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SATURDAY SEPTEMBER 18 1948

TABLE OF CONTENTS

Lowered Incidence of Sensitization with Sulphonamide Combinations
DAVID LEHR, M.D. 543

Purpura Fulminans Complicating Scarlet Fever
T. ANDERSON, M.D., F.R.C.P.Ed., M. S. FERGUSON, M.D., and J. B. LANDSMAN, M.B., Ch.B. 549

Rhabdomyosarcoma of the Urinary Bladder CLAUDE H. VIPOND, M.D., C.M., F.R.C.S.Ed. ..551

Streptomycin in Non-tuberculous Infections CLIFFORD WILSON, D.M., M.R.C.P. 552

"C.B.11": A New Analgesic Drug
W. M. WILSON, M.B., F.R.C.P.Ed., and R. B. HUNTER, M.B.E., M.B., Ch.B., M.R.C.P.Ed. 553

Asphyxia of the Newborn Treated by Rocking
F. C. EVE, M.D., F.R.C.P., and the late N. C. FORSYTH, M.D. 554

Gynatresia: Three Uncommon Clinical Types R. G. MALIPHANT, M.D., F.R.C.S., F.R.C.O.G. .. 555

MEDICAL MEMORANDA

Acute Purpura with Neurological Complications Associated with "Sedormid." W. F. T. TATLOW, M.D. 558

Traumatic Forequarter Amputation. J. D. C. MILLAR, M.B., Ch.B. 559

Poisoning by Ethylene Trichloride. DONALD TEARE, M.D., M.R.C.P. 559

GENERAL ARTICLES AND NEWS

Medicine as a Planned Economy. EDWARD B. HENDRY, Ph.D., M.B. 567

RADIOACTIVE ISOTOPES FOR CLINICAL RESEARCH 569

INDUSTRIAL MEDICINE 570

A Mouth-shield for Use with the Bronchoscope or Laryngoscope. JOHN HALLAM, F.D.S., M.R.C.S. 571

UNIVERSITIES AND COLLEGES 580

MEDICAL NEWS 580

QUESTIONS AND COMMENTS 583

OBITUARY

S. W. Wheaton, M.D., F.R.C.P. 577

A. W. Gill, M.D., F.R.C.P. 578

T. Gwynne Maitland, M.D., D.Phil. 578

S. D. Metcalfe, M.B. 578

H. F. Bell-Walker, M.D. 578

Emrys D. Owen, M.B. 578

D. A. Murray, M.B. 579

Ong Chong Keng, M.B. 579

B. R. Parmiter, M.B. 579

MEDICO-LEGAL

Damages Against Orthopaedic Surgeon 579

LEADING ARTICLES

Safety in Chemical Works 562

Sulphonamide Combinations and Sensitization 563

ANNOTATIONS

Removal of Children's Tonsils 564

Rat-bite Fever 564

Training of Neurosurgeons 565

Biochemical Changes in Hypertension 565

Improvements in Artificial Limbs ...565

Glandular Fever and the Nervous System 566

Rockefeller Benefactions 566

REVIEWS

Malaria 560

Conscience 560

Textbook of Midwifery 560

Uses of Streptomycin 561

Hospital Administration 561

REPORTS OF SOCIETIES

AMERICAN, BRITISH, AND CANADIAN ORTHOPAEDIC ASSOCIATIONS 570

SUPPLEMENT

FREE HOSPITAL PLAN IN THE TRANSVAAL: MEDICAL OPPOSITION *123*

N.H.S. SUPERANNUATION SCHEME *124*

NATIONAL HEALTH SERVICE NEWS *125*

CORRESPONDENCE *125*

H.M. FORCES APPOINTMENTS *127*

B.M.A. LIBRARY *128*

CORRESPONDENCE

Scientific Medicine in Britain To-day. F. M. R. WALSHE, M.D., F.R.S. 572

Globin Insulin—A Criticism. R. D. LAWRENCE, M.D. 572

Streptomycin and Insulin. E. A. WOOD, M.D. 572

Renal Complications in Diabetes. N. G. B. MCLETCHIE, M.D. 572

Diabetic Coma. D. HAMILTON, M.B. 572

Prevention of Dental Caries. SIR LEONARD HILL, M.B., F.R.S. 573

Pioneers of Social Medicine. MAJOR GREENWOOD, D.Sc., F.R.S. 573

Genu Valgum. H. DAVIES, F.R.C.S. ...573

Intravenous Sclerotics. C. E. TAYLOR, M.B. 573

Fibrositis. R. O. ADAMSON, M.D. 573

Fibrositis and the Weather. G. C. PETHER, M.D. 573

Cerebral Aneurysm. G. L. DAVIES, M.R.C.S. 574

Shipping the Sick. B. M. NEWEY, M.B. 574

Stainless Steel Wire. JOHN HOWKINS, M.S. 574

Prevention of Venereal Disease. KATHARINE B. HARDWICK; JOHN SLEIGH, M.B.; W. H. DICKINSON PRIEST, M.R.C.S.; R. C. WEBSTER, M.D.; W. B. LAING, M.B.; R. R. WILLCOX, M.B. 574

Shortage of Nurses. J. R. CROSS; ESTHER CARLING, M.D. 576

Epidemiology Section 582

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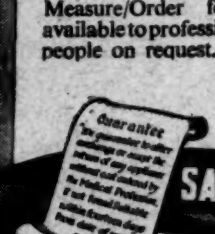

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY SEPTEMBER 18 1948

LOWERED INCIDENCE OF SENSITIZATION THROUGH USE OF SULPHONAMIDE COMBINATIONS*

A NEW CONCEPT

BY

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The incidence of allergic reactions is largely dependent upon the nature of the allergenic substance and the amount and concentration of the antigen to which the individual is exposed. It is also influenced by a great number of predisposing factors such as heredity, constitution, infection, immunization, dysfunction of various organ systems, as well as meteorological and geographical conditions. It is generally recognized that, within limits, the frequency of allergic reactions will increase in direct proportion with the intensity of exposure to the allergen,[1 2 3] particularly in types of sensitization where the role of heredity is less marked. Apparently almost every individual can be sensitized by adequate contact.[4]

There should be little reason to doubt that this rule applies to all drugs that can act as full antigens or haptens, including the sulphonamides. Suggestions of a definite relation between dosage of sulphonamides and sensitization have been made repeatedly almost since the inception of their clinical application,[2 5 6 7] and yet it is still widely believed that the incidence of allergic reactions from the sulphonamides is independent of the dosage used.[8 9]

A critical evaluation of the vast literature on sulphonamide therapy, greatly enriched during the recent war by exacting large-scale studies of the armed Forces here and abroad, gives no support to the assumed independence of dosage and incidence of sensitization. Coburn,[10] for instance, summarizing the tremendous programme of the United States Navy on "The Control of *Streptococcus hemolyticus*" with sulphadiazine, states that "sensitization did not appear to be produced by prophylaxis" even if used for as long as three to six months. His report deals with the experience gained on 600,000 men in approximately 3,000,000 man-weeks with a prophylactic dosage of 1 g. of sulphadiazine daily. The overall incidence of toxic reactions was 0.5% as compared with 4 to 8% of human subjects who develop reactions from therapeutic dosage of sulphadiazine. "Stopping prophylaxis during alternate weeks or alternate months was followed by no increase in the incidence of reactions. Subjects who did not react to the first course of prophylaxis were not sensitive to subsequent courses. The administration of sulphadiazine therapy to a large number of men who had previously tolerated prophylaxis did not cause reactions . . . . There was no difficulty in obtaining a satisfactory therapeutic effect from sulphadiazine in individuals who contracted streptococcal infections while receiving prophylaxis."

Similar points of view were expressed more recently by Rosenberg and Hench[11] from the Rheumatism Centre of the United States Army in their evaluation of sulphonamides for the prevention of rheumatic bouts. These authors, summarizing all reports published in the previous nine years, arrive at the following conclusion: "Theoretical considerations led certain investigators to fear that some patients, treated with small amounts of sulphonamides over long periods, might become 'sensitive' to these drugs and later be unable to take them for other therapeutic purposes. However, no such sensitization was observed. . . . Finally, there was some concern that virulent drug-fast strains of haemolytic streptococci might result from prolonged sulphonamide prophylaxis; no such eventuality has been reported."

It is the purpose of this discussion to demonstrate, with the help of data from the literature on sulphonamide therapy and our own experience with the use of sulphonamide combinations, that the incidence of allergic reactions is dependent upon the dosage of individual sulphonamides. It is further intended to show that the existence of a direct proportional relationship between dosage and production of sensitization may open a rational approach to the diminution in the incidence of drug allergy.

Dosage of Sulphonamides and Incidence of Drug Rash and Fever

In our search of the literature for comparative percentages of sensitization with small, medium, and large dosages of sulphonamides, particular attention was given to sulphanilamide, sulphathiazole, and sulphadiazine because these three drugs have been used most extensively since their introduction into therapy twelve, nine, and eight years ago, respectively, and therefore offer the richest source of comparative clinical data. One can reasonably expect that the findings for these sulphonamides will apply in like manner to other derivatives of the series.

It was realized from the start that clear-cut information could not be expected from so ambiguous and confusing a manifestation of sulphonamide toxicity. The so-called sensitization reactions actually lack any strict standards of evaluation, giving wide leeway to individual opinion and interpretation. It seemed of advantage, therefore, to limit the accounting of allergic reactions to "drug fever" and "rash," which are considered to represent the most common

*This investigation has been aided by grants from the Josiah Macy Jr. Foundation, New York City, and the Schering Corporation, Bloomfield, New Jersey.

indicators of sensitizations. The reservation must be made, however, that the truly allergic nature of these reactions was established by subsequent testing in exceptional instances only. Without such tests drug fever may often be confused with a flare-up of the original disease and many non-allergic skin reactions may be counted as sensitization. This fact seems to have been disregarded by many authors, who consider every rash as sulphonamide allergy and therefore an absolute indication for the interruption of therapy. Otherwise, it is contended, more dangerous signs of sensitization such as hepatitis, "chemotoxic" nephritis, or agranulocytosis may be induced. In this connexion it should be remembered that the allergic nature of these serious but fortunately rare manifestations of toxicity has not been established. In fact, especially with regard to the haematopoietic system, much evidence was presented in favour of a direct and primary tissue toxicity[12] or a depletion of certain essential metabolites or vitamin factors.[13]

A detailed discussion of the pros and cons of allergy versus primary tissue damage is beyond the scope of this paper. It should be pointed out, however, that the intentional omission of extremely rare reactions of disputed nature from this account of sulphonamide allergy will not distort the values to any extent. It should also be clear that such data as can be obtained from the literature on rash and fever undoubtedly contain an appreciable number of non-allergic reactions. Hence, in using the terms "rash" and "fever" interchangeably for sensitization or allergy throughout this discussion I am fully aware of an unavoidable inaccuracy. The figures for true sensitization are probably lower.

An attempt was made to collect data from exacting reports with large groups of patients only; however, no claim of an exhaustive survey is made. Unfortunately, many good therapeutic reports lack clarity in their figures for rash and fever. If these two reactions are listed separately, because either one may occur alone, it would seem imperative to indicate how often both reactions occurred in the same individual in order to avoid overestimations when the total incidence of sensitization is calculated. In all such instances I chose to err on the conservative side by taking only the higher of the two figures rather than their sum and thus to present approximations of the minimum possible incidence. It will be realized in the course of the discussion that the lower figures obtained in this manner for therapeutic dosages tend to disfavour the concept for which these data were compiled. Whenever feasible, the findings of various authors were combined into larger groups. The final data obtained in this manner are summarized in the accompanying Table.

Drug	Daily Dosage in Grammes	Days of Treatment	No. of Cases Treated	Incidence of Rash and Fever	References
Sulphanilamide	1–2	120–240	188	1·0%	15–17
	1·5–4	7–21	1,687	0%	18
	6–9	5–10	1,407	>10·0%	19–20
	Routine therapy*	..	..	7·2%	14
Sulphathiazole	2–4	3–15	3,584	0%	21–26
	6	3–10	2,475	>6·4%	19, 27–33
	6–10	5–10	529	>10·0%	6, 19, 34
	Routine therapy*	..	..	11·2%	14
Sulphadiazine	1	12–90	664,840	<0·5%	35–41
	2–4	3–20	18,185	0·07%	42–45
	4–6	7–14	500	1·8%	46
	6+	2–31	2,791	2·3%	27, 30, 42, 47–52
	Routine therapy*	..	..	2·9%	14

* These figures are based on a comprehensive compilation of the incidence of rash and fever reported in the literature.

For the purpose of correlation, the percentages of rash and fever recently published by Long[14] for therapeutic dosages of the three sulphonamides were included.

The table clearly illustrates a definite relation between dosage and incidence of rash and drug fever. Sulphanilamide given in daily amounts of 1.5–4 g. for 7 to 21 days caused no sensitization in 1,687 patients, whereas 6–9 g. administered for only 5 to 10 days produced reactions in more than 10% of 1,407 patients. Even the worst offender, sulphathiazole, was tolerated without reaction by 3,584 individuals receiving 2–4 g. daily for 3 to 15 days, whereas signs of sensitization were found in more than 10% of 529 patients when full therapeutic dosages were administered for 5 to 10 days. Similarly, sulphadiazine when given in a daily dose of 1 g. to 664,840 men for 12 to 90 days resulted in less than 0.5% overall toxic reactions (with sensitization obviously on a much smaller scale). Even daily dosages of 2–4 g. continued for 3 to 20 days gave an incidence of only 0.07%. Approaching the routine dosage of 6 g. of sulphadiazine and more, the frequency of allergic reactions rises sharply to about 2.3%. The time factor seems less significant beyond the fact that a minimum of three to five days must elapse before allergic reactions begin to appear in any significant number.

These examples may suffice for demonstration of a definite correlation between the dosage of sulphonamide and the incidence of allergic reactions. It could be argued, with justification, that the smallest dosages were used in most instances for prophylactic treatment of healthy individuals, or at least of persons not suffering from acute infections, thus eliminating a possible contributory factor of sensitization. However, this does not apply to the 4 g. daily dosage of any of the three compounds used in the majority of instances for therapeutic purposes. In addition, it was also noted in sulphonamide prophylaxis that larger dosages result in a significant increase in allergic reactions.[53-58] The high incidence of sensitization observed with a 6 g. daily dosage of any of the three sulphonamides could therefore not be explained solely on the basis of a difference in contributory factors. It would seem that a systemic sulphonamide can be administered in a dosage of 1–2 g. daily for long periods of time and even repeatedly[15-17 36-41 53 54] in the same individual without the production of sensitization. The same drug in a dose of more than 4 g. in 24 hours, on the other hand, will induce allergic reactions in a definite and significant percentage of cases. The production of sensitization is apparently dependent upon the maintenance for some time of a certain minimum concentration of the allergen in the tissues which are to be sensitized.

This point of view is supported by many other clinical observations. First, the so-called "non-absorbable" sulphonamides like succinyl sulphathiazole (sulphasuxidine) even if given in large dosages by the oral route, will induce drug rash and fever rather infrequently.[7] Blood levels from these compounds are seldom higher than 1–3 mg. (per 100 ml.). Sulphaguanidine, on the other hand, which is far better absorbed, is known to produce an appreciable incidence of drug rash and fever.[7 59 60] In fact, Smith,[7] who used massive dosages of this compound totalling 142 g. in a 10-day period, reported 21 instances of maculopapular rash among 44 *Shigella dysenteriae* carriers. Blood levels ranged between 10 and 14 mg. per 100 ml., which are unusually high for sulphaguanidine. The sensitization, incidentally, was specific for sulphaguanidine; rash was not produced by sulphathiazole, sulphadiazine, or sulphanilamide. Further evidence for the significance of high sulphonamide concentrations in the production of allergy seems to lie in the fact that sensitization reactions for

local sulphonamide application can be rather frequent[7 62] and as a rule develop only at and around the immediate site of exposure (contact dermatitis), unless there was extensive systemic absorption from this local site.

There is a paucity of exact statements concerning the incidence of sensitization from topical application. Many reports on the use of sulphonamide ointments in pyogenic dermatosis[63-68] do not mention the development of sensitization. Tate and Klorfajn,[69] on the other hand, reported 55 cases of sulphonamide dermatitis among 2,289 admissions to the skin department of a military hospital, and Darke[70] found 12 cases of dermatitis in 218 patients treated with sulphathiazole—an incidence of 5.5%. Northey[7] estimates the average incidence of contact dermatitis from sulphathiazole as 2.2% and compares it with an incidence of 5% dermatitis medicamentosa from the oral administration of this drug.

The wide variations in the incidence of contact dermatitis reported by various authors are probably due in part to the differences in the type of infection treated and the duration of therapy, but are undoubtedly also influenced by the condition of the skin. In many instances the skin is largely intact; hence absorption is at a minimum and sensitization does not occur. However, the eroded areas of eczema, or skin denuded of its protective outer layers by burns or wounds, will permit of deep and extensive sulphonamide penetration. The result may be a high incidence of contact dermatitis.[62] In fact, Lowell[71] recently stated that "allergic reactions were so frequent and severe in eczematous areas of the skin that the prolonged use of sulphonamides on such sites has been cautioned against repeatedly." Systemic readministration of a sulphonamide to patients sensitized locally by previous topical application will often show exclusive or predominant reaction at the locally sensitized area.[70 72-80]

Finally, the dependence of sensitization on absorbability and tissue concentration of sulphonamides can also be inferred from the excellent and exacting study of Sulzberger and associates[62] on human volunteers. These authors investigated the "incidence of dermatitis following treatment with measured amounts of different sulphonamides in the same vehicle, on standard lesions (third-degree burns), in men of the same age group, living in the same environment, on the same diets, at the same occupation, and under similar experimental conditions." The overall incidence of dermatitis was found to be 19% in 254 men. The distribution of sensitization for the four sulphonamides employed was 57% for sodium sulphadiazine, 22% for sulphanilamide, 7% for sulphathiazole, and 5% for sulphadiazine. Based on these remarkable results the authors conclude that "the relative incidence of sensitization corresponded to the relative water solubility of the compounds—the most soluble giving the highest incidence of sensitization." It would seem, therefore, that, especially in systemic therapy, the production of sensitization could be avoided in many instances by preventing the rise of the tissue concentration of any one sulphonamide above a certain definite level. From the data compiled in the Table this tissue level is estimated to lie in the neighbourhood of 5 mg. per 100 ml., allowing for some variations with the different compounds of the series. In this connexion it should be pointed out that in sulphonamide prophylaxis (1 g. of sulphanilamide or sulphadiazine daily) blood levels range between 0.5 and 3 mg. per 100 ml.

However, the production of sulphonamide allergy should not be confused with the response of a sensitized individual in whom a single small dose may elicit a vigorous and typical reaction. It might well be that this fact has contributed to the mistaken conception that the production of sensitization by sulphonamides may occur with small dosages as readily and as often as with full therapeutic amounts. According to Landsteiner's concept,[81] sulphonamides should be considered as haptens or incomplete allergens which obtain the ability to cause sensitization by combining with tissue proteins. In line with this theory, sulphathiazole and sulphamerazine, which possess the greatest protein-binding power, cause high incidences of allergic reaction, although other factors undoubtedly are of importance. (It is known, for instance, that the thiazole ring is more apt to produce sensitization than the pyrimidine ring.) The complete allergen created by combination of a sulphonamide or its metabolite with protein may be highly specific. Individuals allergic to sulphathiazole often tolerate sulphadiazine or other derivatives of the series without reaction. The specificity is also expressed by the substantial difference in the incidence of sensitization reactions established for various sulphonamides. In the majority of human beings apparently the tissue cells are able to distinguish even between closely related sulphonamides with regard to their allergenic properties.[82] In all such instances a combination of several sulphonamides in partial dosages should make it possible to exert full therapeutic effects and yet to "dilute" individual drug concentrations in the tissues below the level at which sensitization reactions are apt to occur. It is obvious that under these conditions the simultaneous presence of several distinct potential allergens in "non-antigenic" concentrations should be of little consequence.

If the cells of the body, on the other hand, do not distinguish between the various sulphonamides the danger of sensitization could still not be greater than if the full therapeutic dosage of a single sulphonamide had been administered. Obviously, the highest possible incidence will be determined by that drug in a combination which tends to induce allergic reactions most frequently. However, there should be no additive or even increased incidence of allergic reactions so long as individual sulphonamide concentrations are kept well below the level necessary for the production of sensitization to any one single sulphonamide in human beings with "normal" susceptibility. This concept seemed to be borne out by our experience with sulphonamide combinations.

Sulphonamide Combinations and the Incidence of Sensitization

Since 1944 unselected patients of all age groups suffering from acute bacterial infections have been treated with various combinations of sulphonamides at the Flower and Fifth Avenue Hospitals, as well as at the Metropolitan Hospital on Welfare Island. Adhering initially to the common belief that sulphonamide dosage is of little consequence with regard to the incidence of allergic reactions, we were on the look-out for an increase in sensitization.[83] Instead, however, we found a definite and significant decrease in the incidence of drug rash and fever, and no serious untoward reactions.[83-86] Up to the present time more than 1,000 patients have received treatment with sulphonamide combinations at the hospitals associated with our institution. Although reports of allergic reactions in this series were sporadic on the whole, I have included for evaluation in the present paper only patients who were under my direct supervision or that of my immediate associates. Their number totalled 610. Of these, 393 were treated with a mixture of sulphadiazine and sulphathiazole, 160 underwent therapy with a combination of sulphadiazine and sulphamerazine, and 57 were treated recently with various combinations of three sulphonamides. Equal partial amounts of the different sulphonamides were employed in all instances by the oral or subcutaneous route. Reactions

attributed to sensitization were observed in 11 cases, making it an overall incidence of slightly less than 2%. The distribution was as follows: sulphadiazine–sulphathiazole combination, 8 cases (2%); sulphadiazine–sulphamerazine combination, 2 cases (1.25%); sulphadiazine–sulphamerazine–sulphapyrazine combination, one instance of rash, apparently not allergic.

Four patients showing drug fever and/or rash were tested subsequently with small dosages of the sulphonamides to which they had been exposed. Two of these had developed allergic symptoms during therapy with the sulphathiazole–sulphadiazine combination; however, both proved to be sensitized only to sulphathiazole and not to sulphadiazine. A third patient showed no reactions while on intensive therapy with the sulphadiazine–sulphathiazole combination. Several days after discontinuation of therapy 4 g. of a combination containing sulphadiazine–sulphamerazine–sulphathiazole was administered for the purpose of an absorption-excretion study. Rash, fever, and general malaise were observed within a few hours after administration, clearing completely within 36 hours.

Subsequent testing with the separate sulphonamides in the above-named order revealed, as in the first two instances, sensitization only to sulphathiazole, whereas sulphadiazine and sulphamerazine were tolerated without reaction. Finally, a patient with brucellosis treated intensively with a combination of sulphadiazine–sulphamerazine–sulphapyrazine (blood levels of 12–20 mg. per 100 ml. free sulphonamide), in addition to intermittent intramuscular injections of streptomycin, developed a confluent maculopapular rash over the entire body in the fourth week of treatment. Temperature at that time was continuously subfebrile. The emergence of the eruption was not accompanied by malaise or a febrile reaction. All therapy was stopped and the rash disappeared within 48 hours with residual light pigmentation. At this stage 0.5 g. doses, first of the separate and then of the combined sulphonamides, were administered at 24-hour intervals. Finally, one intramuscular injection of streptomycin was given. All drugs were tolerated without reaction. Temperature fell to normal and the patient was discharged as cured.

It is obvious from these examples that two sulphonamides can be given simultaneously without the development of sensitization to both drugs. The fourth case illustrates that in many instances reactions may be counted as allergic without sufficient evidence for such a contention. Apparently the rash in this patient constituted a primary toxic response of the skin to intensive and prolonged exposure to sulphonamides or streptomycin. Dermatoses caused by hypersensitization should always be differentiated from toxic non-allergic dermatitis caused by overdosage or accumulation of a variety of agents.[87]

It should also be kept in mind that sensitization to several or all compounds of the sulphonamide series (group allergy) may develop in some individuals from the use of any one single representative of this group of drugs.[82] Obviously, if any such person develops group allergy during treatment with sulphonamide combinations it would not necessarily prove that sensitization to all components of the combination was elicited by their simultaneous administration.

The low overall incidence of rash and fever (2%) that we observed in our patients treated with sulphonamide mixtures speaks against a simple summation of such reactions by employing combinations of several sulphonamides in partial dosages. Otherwise we should have observed an incidence in the neighbourhood of 10%, since more than 400 of our patients received combinations containing sulphathiazole. Actually, then, our findings indicate a significant reduction rather than an increase in the incidence of sensitization. The most plausible explanation seems to lie in the lowering of individual sulphonamide concentrations in the tissues beyond the critical level necessary for the production of allergic reactions. It will be remembered that this concept was postulated earlier in this paper on the basis of the experience of many authors with single sulphonamides.

For clinical purposes a daily dosage of 2 g. of any sulphonamide seems to lie safely below the amount that would produce sensitization, except in rare instances with special hypersusceptibility. Thus a combination of three therapeutically equivalent sulphonamides would allow a daily dosage of 6 g. at a substantially reduced risk not only of renal damage but also of sensitization. If this concept proves correct the introduction of more than three sulphonamides into a combination should further increase the safety of sulphonamide therapy.

Comments

The clinical use of sulphonamide mixtures, although widely accepted to-day on the basis of the protection afforded the kidney, is still too recent to permit any decisive statement on the question of sensitization. Our own limited experience would seem sufficient to disprove the contention of an increase in the incidence of allergy by the proper employment of combined sulphonamides. The concept of a reduced incidence, however, requires confirmation by other authors and with larger series of patients.

Of the few clinical reports on sulphonamide combinations which have been published thus far from other institutions,[88-92] only the one by Zeller, Hirsh, Sweet, and Dowling,[92] reporting on the combined use of sulphadiazine and sulphamerazine in 75 patients with meningitis, attempts to demonstrate a possible increase of allergic reactions. Unfortunately, these authors arrive at conclusions which are not supported by their own results but are based on the fallacious interpretation of statistical data. Since their point of view is diametrically opposed to our concept, the evidence which Dowling and his associates present in support of their contention deserves close scrutiny.

One is struck by the unusual combined tabulation "drug fever and/or conjunctivitis, drug rash and/or conjunctivitis," which seems to attach undue significance to conjunctivitis alone as a sensitization reaction. Obviously the combined reporting of these three reactions makes it impossible to elucidate the exact position of conjunctivitis in the overall picture of reactions counted as allergic in nature. However, it seems reasonable to assume that the exceptionally high figure for sensitization reactions reported by Dowling and his co-workers for sulphadiazine (10%), which is in conspicuous contrast to all reports in the literature, is due to the inclusion of conjunctivitis as an allergic reaction.

Although conjunctivitis is seen occasionally during sulphathiazole therapy, it seems extremely rare from sulphadiazine and homologues.[7] Plummer and Wheeler[4] reported one case of conjunctivitis among 1,357 patients receiving full sulphadiazine therapy without qualifying the nature of this reaction. Other authors reporting toxic reactions from sulphadiazine or sulphamerazine do not mention the occurrence of conjunctivitis. Dowling himself saw no conjunctivitis in 137 patients with pneumococcal pneumonia treated with sulphadiazine.[93] We have not observed any instance of allergic conjunctivitis in our large series of patients treated with sulphonamide combinations. Incidentally, no statement is contained in Dowling's report whether any attempt was made to establish the allergic nature of conjunctivitis, which is a well-known and frequent

concomitant sign of meningitis. Furthermore, Dowling *et al.* increased the dosage of the combination arbitrarily by "25 to 33%" above the generally accepted routine dosage of sulphonamides. Thus adult patients received 8–9 g. of the sulphadiazine–sulphamerazine combination daily, as contrasted with the 6 g. maintenance dose used by these authors in previous series with the separate compounds. Consequently each patient on combination therapy received an additional amount of at least 21 g. of sulphonamide in the average 10-day treatment period.

While the authors neither claim nor prove the necessity for such a substantial increase in dosage when using the sulphadiazine–sulphamerazine combination, they formulate their conclusions on the advantages and disadvantages of mixture therapy as if they had used the ordinary required dosage, and thus present an entirely misleading picture. Apparently based on the prevailing point of view that the incidence of sensitization is independent of dosage, Dowling and his associates attempt to demonstrate statistically significant differences between the sulphadiazine–sulphamerazine combination and the separate compounds with complete disregard of the fact that the combination was used in a substantially higher dosage range. If we assume that the tissue cells were unable to distinguish between sulphadiazine and sulphamerazine, then an 8–9 g. daily dosage of the combination which produced the highest blood levels should be expected to result in a higher incidence of allergy than either compound at a 6 g. daily dosage. Even if, on the other hand, sulphadiazine and sulphamerazine had acted as two distinct and specific haptens an excessive dosage of the combination could have obviously created sensitizing tissue concentrations for both sulphonamides. The median blood levels obtained by Dowling *et al.* (7.6 mg. per 100 ml. for sulphadiazine, 11.0 mg. per 100 ml. for sulphamerazine, and 14 mg. per 100 ml. for the combination) illustrate this possibility very clearly. In either instance an increase in the percentage of sensitization would not be surprising and would obviously not prove the point that these authors had tried to make. In this connexion it should be remembered that they did not report a statistically significant increase of sensitization with the sulphadiazine–sulphamerazine combination. In conclusion, then, the results of Dowling and his associates are explainable on the basis of the substantially higher dosage schedule of the combination and therefore carry no weight against the concept under discussion.

The recognition of a direct proportional relation between the dosage of individual sulphonamides and the incidence of allergic reactions poses many new questions which far exceed the scope of this limited discussion. To mention only a few, it should be investigated whether sulphonamides which are structurally less closely related (like sulphadiazine and sulphacetamide) are more apt to be distinguished by the cells of the body as specific allergens than isomers or homologues (sulphadiazine, sulphapyrazine, and sulphamerazine). A positive finding would obviously influence the selection of sulphonamides for use in combinations. Consideration should also be given to the possible diminution of toxic manifestations other than those due to sensitization or crystalline deposition in the kidneys.

Sulphapyridine, abandoned as too toxic in full therapeutic dosage in the United States, and sulphathiazole, under consideration for elimination,[94] should be re-examined in the light of this concept. Both are highly potent chemotherapeutic agents with an excellent record of efficiency, especially in pneumococcal and staphylococcal infections, respectively. The inclusion of either drug in partial dosage into triple combinations with sulphadiazine and sulphamerazine should lower the incidence of their untoward reactions to a substantial degree. In addition, the *in vivo* antibacterial efficiency of such combinations should equal, if not surpass, that of any one single sulphonamide.

Finally, the investigation should be extended to include manifestations of sensitivity elicited by many other drugs. It is known, for instance, that the principal toxic reactions from thiouracil are granulocytopenia, leucopenia, drug fever, and dermatitis.[95] Recently Cookson and Staines,[96] reviewing four years' experience with thiouracil, stated that "most toxic effects were seen when the daily dose exceeded 0.1 g." They found a decline in the incidence with the use of smaller doses. A similar suggestion was made by Williams and Clute.[97] McGavack and associates[98] believe that the incidence of agranulocytosis from thiouracil can be decreased by avoiding excessive dosages. Others[95 99] fail to find a dependence of the incidence of toxic reactions upon dosage within the therapeutic range. It seems important to point out that in these instances dosages varied as a rule within the fairly narrow range of 0.4 to 0.8 g. thiouracil in 24 hours. In this connexion it is interesting to note that propyl thiouracil, which is effective in one-third the dosage of thiouracil on a weight basis, causes only 1.6% toxic reactions as compared with 9% for the latter drug.[100] This substantially lower toxicity of the propyl homologue, which is quite generally agreed upon,[101-105] has been attributed to the appreciably lower dosage schedule of this compound.[106] It has also been established that many patients sensitized to thiouracil can be continued on therapy with propyl thiouracil[101-104] or methyl thiouracil[96] without showing any ill effects. These observations suggest the possibility of lowering the incidence of dermatitis and fever and other toxic reactions occurring under therapy with full dosages of any one compound of the thiouracil series by using appropriate combinations of several homologues in partial dosages. Generally speaking, it should be feasible to diminish the incidence of certain untoward reactions from many drugs by employing partial amounts of therapeutically equivalent drugs of different molecular structure in combination instead of the full dosage of any one compound.

Summary

Perusal of the extensive literature on sulphonamides reveals that, in the dosage range employed in human prophylaxis and therapy, the incidence of drug rash and drug fever increases in direct proportion with the dosage of absorbable sulphonamides.

At an oral dosage of not more than 2 g. of sulphonamide in 24 hours none of the compounds used at present appears to produce rash or fever in any significant percentage of cases even if used for prolonged periods and repeatedly in the same individuals.

The incidence of these reactions assumes significant proportions when the dosage is increased to more than 4 g. in 24 hours, and reaches even higher percentages with full therapeutic amounts of 6 g. or more in 24 hours, provided medication is maintained for a minimum of three to five days.

These observations indicate that the production of so-called sensitization reactions is dependent upon the repeated presence of certain critical tissue concentrations of a sulphonamide for a minimum period of several days.

In the majority of patients sensitization is specifically limited to the sulphonamide used for therapy. Hence the simultaneous administration of several sulphonamides in partial dosage should result in a reduced incidence of sensitization because it permits "dilution" of individual drug concentrations below the level necessary for the production of allergy.

Practical experience with combinations of two or three sulphonamides in 610 patients demonstrated a conspicuously low incidence of drug rash and fever at the full therapeutic dosage of 6 g. in 24 hours.

The significance of this finding and its possible bearing upon toxic reactions from compounds of the thiouracil series, and drug allergy in general, are discussed.

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The University of Sheffield has just issued in the form of attractively bound pamphlets a number of inaugural lectures delivered by newly appointed professors over the period 1945–7. Professor C. H. Stuart-Harris lectured on "The Fight Against Infection"; Professor C. P. Beattie on "The Universities, Bacteriology, and National Health"; Professor D. H. Smyth on "The Role of Physiology in a Scientific Education"; and Professor H. A. Krebs on "The Advent of Biochemistry." Copies may be obtained from the Registrar, price 1s. 3d. post free.

PURPURA FULMINANS COMPLICATING SCARLET FEVER

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A haemorrhagic form is described for each of the infectious fevers. Such illnesses are usually the most severe types, and the haemorrhages occur as a manifestation of the acute stage of the disease. Much less frequently the appearance of haemorrhages complicates an already established convalescence. The following case is illustrative of the latter form.

Case History

A girl aged 9 complained of sore throat on Sept. 15, 1947. Next day her family doctor, on the appearance of a typical rash, diagnosed scarlet fever and had her isolated in her own home. Her temperature was high and she was moderately ill for a day or two, but the course was uneventful and no specific therapy was considered necessary. In particular no serum was given and no sulphonamide was ordered then or later. During the first week of illness some oedema of the eyelids was suspected, but examination of the urine showed no abnormalities.

Progress was thus uneventful until Sept. 26, when complaint was made of severe abdominal pain of sudden onset. The patient vomited. The left forearm and elbow-joint suddenly became swollen and tender. Next day haemorrhagic areas were noticed on the lobes of both ears and on the lower lip. Further haemorrhages appeared on the 28th, and by this time the clinical condition had deteriorated so severely that admission to hospital was sought.

On admission the temperature was 97° F. (36.1° C.), pulse 140, and respirations 24. The child was pallid and was obviously extremely ill. The tongue was furred but moist. The throat showed numerous petechial haemorrhages on the soft palate and the tonsils were enlarged, of purplish colour, and oedematous from haemorrhage. There was a small ulcer on the inner surface of the left cheek. The lower lip and the surrounding tissues were grossly swollen and were involved in a large subcutaneous haemorrhage. Ecchymoses were also present in the lobes of the ears, on the right hand, and on the buttocks. Both elbow-joints were swollen, and movement was restricted. There was surrounding ecchymotic staining. Petechial haemorrhages were also noted on the trunk. Elsewhere the skin showed a fine pin-hole desquamation; and if there had been any doubt about the original diagnosis the typical appearance of the desquamation would have permitted a retrospective diagnosis of scarlet fever.

At this time there was little else of note in the examination, except that the tip of the spleen was palpable: but four hours later a considerable deterioration was noted. Fresh haemorrhages had occurred. The patient's colour was grey and she was obviously shocked. The abdomen was slightly distended and tense. The liver was now enlarged but not tender and the spleen was easily palpable. There was no tenderness in either subcostal angle. The systolic blood pressure was 90 mm., but the diastolic was unrecordable. The pulse was thin and thready.

On admission the patient had had the usual specimens (including a blood culture) withdrawn for examination and had been given 100,000 units of penicillin, since it seemed possible that the condition was a streptococcal septicaemia complicating scarlet fever. The rapid changes which occurred in the next few hours made it apparent that the correct diagnosis was a fulminant purpura. Accordingly, after further specimens were removed, 5 ml. of cortical suprarenal extract was given along with 500,000 units of penicillin, and these were repeated at four-hourly intervals. The question of a blood transfusion was carefully considered, but because of the risk of reaction it was decided not to give one; and, indeed, the patient's condition seemed so critical that no chance of recovery could be entertained.

The improvement 12 hours later was therefore striking and unexpected. No fresh skin haemorrhages had occurred. She was now more alert and was interested in her surroundings. Further vomiting had, however, occurred and the specimens contained altered blood. The pulse was still of poor quality, but the systolic blood pressure could be recorded more easily, and varied between 95 and 100 mm. The abdomen remained tense and the liver and spleen were enlarged. Examination of the urine showed granular and hyaline casts and a large number of erythrocytes. On the evening of the 29th a few fresh skin haemorrhages were noted. By the 30th the patient was progressing satisfactorily, and although convalescence was slow the subsequent course was uneventful. The bowels were kept constipated during the first five days in hospital. At the end of this time a gentle wash-out resulted in the return of typical melaena stool. During convalescence normal results were obtained from tests undertaken to ensure that suprarenal function was satisfactory, and the patient was discharged on Nov. 10. When she reported back two months later she was still somewhat anaemic, but was otherwise normal. In March, 1948, she was well in all respects.

The laboratory findings are shown in the accompanying Table. From these it will be seen that the blood culture taken on admission was sterile. There can be little doubt that she had lost a considerable amount of blood on admission and that as a result there was a moderate degree of haemoconcentration. Platelets were always found, and although the figures are low

Laboratory Findings.

	September			October								
	28	29	30	1	2	3	4	6	8	10	13	17
Haemoglobin (g. %)	15·9	14·0	11·8	10·4	10·3	11·3	10·5	8·2	8·7	9·0	8·9	9·6
Red blood cells (millions)	4·6	4·83	4·54	3·54	3·37	3·65	3·48	2·67	3·23	3·15	3·79	3·67
Reticulocytes (%)	2·4	5·0		7·0	4·6	4·2	3·2	1·4	1·0	4·2	2·0	0·6
Platelets (thousands)	100	120	143	280		260	140	159		270		
Packed cell volume	50	45	30	35	33	34·5	35	28	29	29	30	31
White blood cells (thousands)	20	13·2		7·8	3·8	5·0	5·2	4·2	4·8	10·0		
Neutrophils (%)	85	87		88	77	70	43	45	65	81		
Mononuclears (%)	15	13		12	23	30	57	55	35	19		
Plasma proteins (g. %)	5·0	5·5		4·8		5·3	4·1	5·8	5·7			5·8
Blood culture	No growth											
Bleeding time (minutes)	2·5											
Sternal marrow	+											
Clotting time (minutes)	3·0											
Prothrombin time			70%									
Urine:												
Red blood cells		++			+	+	0			0		
White blood cells		++			+	+	+			0		
Casts		+				++	+			0		
Therapy:												
Penicillin (million units)	0·6	3·0	2·5	1·5	1·5	1·5	1·5	0·5	0·3	0·3		
Eucortone (ml.)	10·0	30·0	12·0	6·0	6·0							
D.O.C.A. (mg.)						10·0						

the important fact is the demonstration of their presence. A sternal puncture was performed, but the specimen obtained only permitted the examination of films. No significant defect was noted; there was an abundance of megakaryocytes.

Discussion

Purpura is not a common complication of scarlet fever; indeed, it is interesting to comment that the last case recorded in Glasgow (Pratt and Frew, 1929) was also seen at Knightswood Hospital. Gibson and Hobson (1932) have described two fatal cases, both from the same family. Box (1933), who reviewed the subject of haemorrhage in acute fevers, suggested that the toxin produced a capillary lesion, which in most cases, however, was transitory. He considered that the acute glomerulonephritis of scarlet fever might be a local manifestation of this same lesion. Fox and Enzer (1938) have described four cases, two of them fatal. No enlargement of spleen or liver was noted in any of their patients, and haematological examinations were not significant of any particular disease process. Necropsy revealed no evidence of intravascular clotting, but there were microscopical extravasations of blood. In one of the patients who recovered a progressive anaemia developed.

Now, in any acute infection the occurrence of haemorrhage during the stage of the primary illness is not hard to understand, for at this time the presence of an acute infective condition with tissue destruction and generalized toxin diffusion might well induce either central changes in the blood-forming organs or damage to the endothelium of the terminal vascular channels. It is more difficult to understand why such a complication should manifest itself in a patient who has already reached a stage of convalescence. Three possibilities require consideration, the first of which can in the present case be immediately dismissed.

First, the frequent administration of sulphonamides, even to cases of mild infection, might induce some state of sensitization which would favour capillary damage. Two patients who developed purpura during convalescence from a streptococcal infection have been recorded by Rantz, Boisvert, and Spink (1945). Both had received a sulphonamide—one nine days and the other 36 days before the appearance of haemorrhage—and the authors comment that the administration of the drug confused the picture in regard to aetiology. In our patient such an explanation can be discountenanced, for it is definitely known that no medicaments were used.

The second possibility to be considered is that the condition arises from some form of sensitization induced by the original infecting agent. Any discussion of the pathogenesis of the late complications of scarlet fever, such as nephritis and non-suppurative arthritis, must take into consideration the fact that in neither is there obvious clinical evidence of an infective condition at the time when the complication arises. It would seem possible that the organism and its toxins might set up tissue reactions during the acute stage of the illness which would induce a state of hyper-reactivity, but such a hypothesis would give rise to the further suggestion that before the acute manifestations of the complication appeared some secondary stimulus to the sensitized mechanism must be applied. In recent years various workers—e.g., Gunn and Griffith (1928), Allison and Brown (1937), and De Waal (1940)—have drawn attention to the frequency with which reinfection occurs in scarlet fever wards, and such reinfection might well supply the stimulus required. In this respect it is interesting that Ehinger (1945) has shown that cases of nephritis occurred more often in individuals who had acquired during convalescence a secondary infecting type of streptococcus, and that the onset of nephritis rapidly followed the reinfection. In the present case it seems unlikely that such an explanation can be supported, for the patient was nursed at home, in isolation, during the course of the illness. Cross-infection by a different streptococcal strain, though not impossible, is certainly improbable.

The third possibility is that after apparent recovery the original organism remains in some nidus in a state of uneasy equilibrium with the host, and that the constant slow absorption of toxic products induces gradual changes of a sensitizing nature in certain organs. Although the old theory of "septic foci" has fallen into abeyance, the experience of those who see numbers of unexplained fevers would suggest that it is certainly true that in some of these cases cure may be obtained only after the eradication of some focal sepsis which has given rise to no clinical symptoms whatever.

In the American literature the focal lesion in such cases of purpura occurring in convalescence from infection is often described as a diffuse endotheliosis (Fox and Enzer, 1938). The use of this vague term (which in no way explains the pathogenesis) infers that the condition is not primarily infective but rather is toxic in origin. Our experience with the case which we have described gives some ground for the belief that a continuing infective element may play a part in the aetiology, for the most surprising feature was the amazing degree of recovery which ensued when the body was subjected to massive penicillin therapy. We are aware that mild cases of convalescent purpura have recovered in the past, but we would emphasize that the condition of our patient on admission was grave and that death seemed imminent. Her startling improvement within 12 hours of the beginning of treatment would suggest to us that the administration of penicillin had controlled some latent infective process which was inducing the vascular damage. The presence of thrombocytes throughout, although admittedly at a low level, would argue that the haemorrhages were not due to any deformity of the clotting mechanism itself; and the state of the bone marrow, too, indicated that there was no primary damage of the haemopoietic system.

It seems to us that there is only one other diagnosis to be considered. It might be suggested that the condition was an acute fulminating meningococcal septicaemia with suprarenal apoplexy. Against such a diagnosis we can only aver that the blood culture was sterile; that tests in convalescence failed to show permanent damage to the suprarenals; and that, nursed in the early stage at home in isolation, contact with a meningococcus seems unlikely. It is more probable that the cortical extract administered had merely overcome a temporary deficiency, for had the suprarenal damage been extensive one would have expected the patient to require a maintenance form of therapy.

Summary

A case of purpura fulminans (non-thrombocytopenic) complicating the convalescence of a case of scarlet fever is described. The patient recovered. It is suggested that the possibility of a continuing or a reintroduced infection must be taken into account in a consideration of the pathogenesis of such conditions.

We wish to thank Professor D. F. Cappell, Pathology Department, Glasgow University, for his report on the sternal marrow films.

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RHABDOMYOSARCOMA OF THE URINARY BLADDER

BY

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Rhabdomyosarcoma of the urinary bladder is a rare tumour the characteristics of which have been well reviewed by Khoury and Speer (1944). These writers have found eight cases in the literature, to which they have added a further case. A tenth (the first in this country) has been reported by Minchin (1947). Here is the report of a further case.

Case Report

A 21-months-old male child was admitted to hospital on June 1, 1947, having had retention of urine for twenty-one hours. The child had been healthy in all respects and had had no previous complaints before the onset of retention. At the time of admission there was some overflow incontinence, the bladder was apparently distended to the level of the umbilicus, and the child was in pain. A skiagram of abdomen and pelvis showed no opaque urethral calculus. After catheterization a firm mass was felt rising from the pelvic cavity to the level of the umbilicus. A tentative diagnosis of tumour of the bladder wall was made.

On June 5 a suprapubic cystotomy was performed by Mr. J. W. Riddoch under general anaesthesia. Exploration of the bladder revealed a firm smooth tumour occupying the posterior wall of the bladder and pushing that organ forward. The internal urethral meatus could be defined, and seemed to mark the lower limit of the growth. The impression was that this growth was covered only by the mucosa of the posterior bladder wall. On attempted biopsy the haemorrhage was severe. A de Pezzer catheter was inserted and the bladder wall closed in layers. The case was now considered to be one of myosarcoma of the bladder wall.

The patient became progressively emaciated and died of cachexia on Oct. 26—just under five months from the onset of symptoms. During the last few weeks of his life the suprapubic opening would no longer accommodate a catheter, and he discharged his urine through a narrow fistula.

One month before death his red cell count was 4,770,000, white cell count 13,950, and haemoglobin 71%. His erythrocytic sedimentation rate was a .63-mm. fall in the first hour (Westergren technique). His blood urea at that time was 28.57 mg. per 100 ml. During most of his illness the patient's temperature ranged from 99 to 99.8° F. (37.2–37.7° C.), but there were five or six periods of seven to ten days each in which the temperature fluctuated around 102° F. (38.9° C.). These probably coincided with exacerbations of his pyelonephritis.

Necropsy (Oct. 27).—A large tumour (Fig. 1) weighing about 1,788 g. occupied and completely filled the pelvis, extending to the level of the umbilicus. The tumour was entirely extraperitoneal. On macroscopic examination its surface was lobulated and the cut surface varied from clear gelatinous areas to others which were yellowish white and of firm consistency. There were some necrotic areas and slight interstitial haemorrhage. The peritoneal cavity contained about 50 ml. of blood-stained effusion. The visceral peritoneum was studded with small secondary nodules, especially marked in the great omentum. There were very few adhesions. The terminal part of the pelvic colon and the rectum were surrounded by growth, which appeared to have invaded their walls. The left lobe of the liver contained one large and several smaller metastases. The right lobe had several small metastases. Both kidneys were enlarged. The left showed a definite pyonephrosis and the right a hydronephrosis. The ureters were dilated and obstructed by the growth. Both ureteric orifices were found to be free from growth and there was no evidence that the walls of the ureters had been invaded. The bladder contained purulent urine. Both testes and spermatic cords were normal.

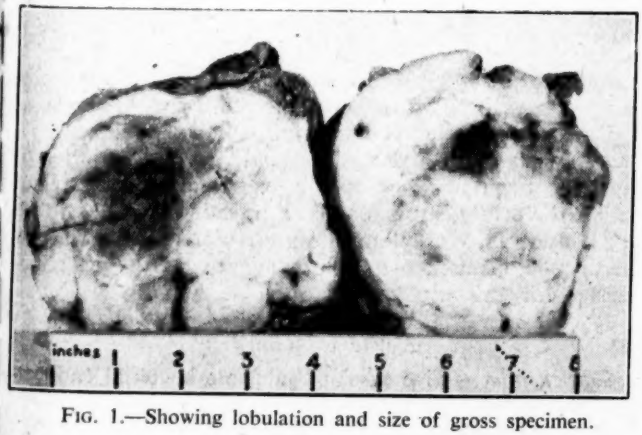

FIG. 1.—Showing lobulation and size of gross specimen.

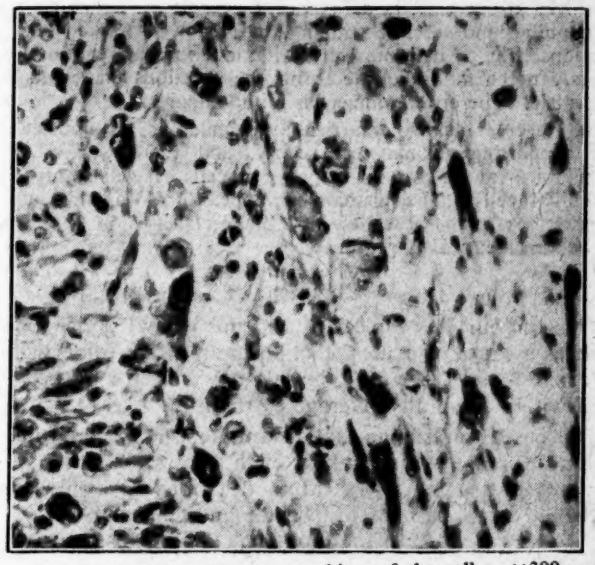

FIG. 2.—Showing the pleomorphism of the cells. ×300.

Histological Report.—Microscopical section of the tumour showed it to be richly cellular (Fig. 2). The cells were polymorphic and most of them had an oval nucleus with a prominent nucleolus and a well-marked chromatin network; the cytoplasm varied from a long rectangular type in some cells to a small perinuclear rim in others. There were also multinucleate forms containing two or three nuclei with a wide band of cytoplasm often

FIG. 3.—Showing the well-marked cross-striations. ×450.

prolonged at one side. In all cases the cytoplasm was markedly eosinophilic, and suitable staining revealed well-marked cross-striations (Fig. 3) in some cells, with longitudinal striations in others. In the multinucleate forms the striations tended to be concentric. There were numerous mitotic figures.

The vascular supply was rich and tended to be sinusoidal. The supporting stroma was scanty, and there was a rich reticulum arranged around columns of cells as well as around individual cells. The histological appearance was that of a rhabdomyosarcoma. Sections of the metastases in the liver showed an identical appearance.

Comment

This tumour was typical of its kind in that it presented itself as a cause of acute retention in an infant (of 11 cases reported 8 have occurred in infants) and that it proved fatal within 5 months (average 6½ months).

This case is unusual in that distant metastases were found. Their structure was identical with that of the tumour. Distant metastases have been described in only one preceding case—that of Mackenzie and Chase (1928).

I wish to thank Mr. J. W. Riddoch, honorary surgeon, in whose charge this patient was treated, for encouragement to publish this case; Dr. A. G. Marshall, pathologist to the Corbett Hospital, who performed the necropsy and supplied the histological report; and Dr. W. Whitelaw, Birmingham, who kindly provided the micro-photographs, and who permits me to say that he agrees with the diagnosis.

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STREPTOMYCIN IN NON-TUBERCULOUS INFECTIONS

SUMMARY OF A REPORT TO THE MEDICAL RESEARCH COUNCIL

BY

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In December, 1946, the Medical Research Council appointed a committee* to arrange clinical trials of streptomycin in non-tuberculous infections, in parallel with the trials in certain forms of tuberculosis which have been organized by another committee of the Council. The trials in non-tuberculous infections began at five centres in London and later were extended to eleven centres throughout the country. This report summarizes the pooled results of the investigation; more detailed results will be published by individual observers. Because of the small amounts of streptomycin available, the relative rarity of suitable cases, and the wide diversity of conditions treated, experience of most infections in which streptomycin therapy may be effective is still limited. Even when, as in *Haemophilus influenzae* meningitis, a reasonably large series has been studied, the distribution of cases over so many centres has led to unavoidable variations in case selection, therapeutic procedure, and bacteriological control. For these reasons present claims must be guarded. Nevertheless, some clear-cut results have been obtained and profitable lines for further inquiry have been indicated.

These trials have been restricted to infections resistant to other forms of therapy in which bacteriological control of treatment has been possible. With few exceptions the infecting organism has been proved streptomycin-sensitive before treatment has been begun; occasionally—e.g., in infective endocarditis—when penicillin treatment has failed, subsequent attempts to isolate the organism have been unsuccessful.

The chief value of streptomycin (apart from tuberculosis) lies in the treatment of penicillin-resistant infections due to the Gram-negative bacilli, particularly *H. influenzae*, *Proteus*, *Pseudomonas pyocyanea*, and *Bact. coli*. The clinical disorders in which treatment has been most effective are septicaemias, meningitis, urinary-tract infections, and local (superficial) infections.

H. Influenzae Meningitis

The results of preliminary trials in the United States suggested that streptomycin might be particularly valuable in this condition; a standard scheme of treatment was therefore recommended in the present investigation.

Dosage.—Intramuscular, 20 mg. per 1 lb. (0.45 kg.) body weight daily in divided (four-hourly) doses; *Intrathecal* (in saline), 50–100 mg. initial dose, according to age, and 25–50 mg. on subsequent days. Treatment was continued for at least seven days after cerebrospinal fluid became sterile.

Results.—Forty-three cases were treated with streptomycin. Four of these also received sulphonamides, penicillin, or serum; in five others the C.S.F. was reported sterile before streptomycin injections were started. Of the remaining 34 cases, the infection was controlled in 25 (74%), while treatment failed in nine. There was no significant difference in age, duration, or C.S.F. changes between the two groups, but clinically the unsuccessful cases appeared to be more severe. Where typing was carried out the organism was found to be Pittman type b. When treatment was successful the C.S.F. usually became sterile within 24 hours of the first intrathecal injection. Streptomycin was effective in 13 cases which had relapsed on other treatment and in nine cases in which the infection had been present for two weeks or longer. Four patients relapsed after an initial response to streptomycin, but the organism remained sensitive and further treatment with streptomycin alone was successful. The principal cause of failure was the development of resistance by the organism; this occurred in seven of the nine failures, sensitivity changing from 0.5 to as high as 5,000 units in one to four days.

From this series it appears that streptomycin alone is probably as effective in *H. influenzae* meningitis as any other form of treatment at present available. The development of resistance is, however, a serious drawback, and it has been decided in future trials to use a combination of streptomycin, penicillin, and sulphonamides from the start.

Other Forms of Meningitis

Fourteen cases of meningitis due to penicillin-resistant bacteria have been treated with streptomycin. The causative organisms included *Bact. coli*, *Ps. pyocyanea*, *Staph. pyogenes*, *Proteus*, and *Str. faecalis*. In the majority of cases the meningitis developed after operation for cerebral abscess or cerebral tumour. The infection was controlled in 11 instances. Streptomycin is therefore a valuable new therapeutic agent in pyogenic meningitis due to penicillin-resistant organisms.

Other Infections

Septicaemias.—Five cases of subacute bacterial endocarditis due to *Str. viridans* or *H. influenzae* and one case of uncertain nature have been treated. With the exception

*Professor Sir Alexander Fleming (chairman), Professor Ronald V. Christie, Professor L. P. Garrod, Mr. R. Vaughan Hudson, Professor H. Raistrick, Dr. Robert Cruickshank, Dr. F. C. O. Valentine, Dr. F. R. Selbie, Professor Clifford Wilson (secretary).

of the latter, the response to streptomycin has been only temporary. Two cases of septicaemia without endocarditis due to *Ps. pyocyanea* or *Bact. coli* have responded satisfactorily.

Urinary-tract Infections.—A series of 61 patients with urinary-tract infection due to *Bact. coli, Ps. pyocyanea, Proteus, Staph. pyogenes,* and *Str. faecalis* has been investigated in 10 centres. In roughly half the cases the infection has been controlled by intramuscular administration of 3 g. of streptomycin daily for one to three days. Failure has almost always been due to the development of resistance. As with other antibacterial agents, streptomycin has a limited value where there is some underlying condition which is apt to lead to recrudescence of the infection.

Local Sepsis.—Fifty-five patients with local infections have been treated. These include a wide variety of lesions such as infected burns, operation wounds, superficial ulcers, sinuses, abscess cavities, and septic skin conditions. The bacterial causes were similar to those detailed in the preceding paragraph. Daily applications of a saline solution of streptomycin (2 mg. per ml.) have been used either alone or combined with intramuscular therapy. The results are favourable, particularly in superficial lesions, provided that all necrotic tissue is removed. The employment of a standard technique is essential. Streptomycin has been used effectively as a cover for skin-grafting. In a proportion of cases failure has been attributable to the development of resistance.

Respiratory Infections.—Chronic lung infections due to bronchiectasis and lung abscess (14 cases) have been treated by inhalation and intramuscular injection. Although a temporary reduction in bacterial content of the sputum has been noted the cases showed little if any clinical improvement. The results of a preliminary trial in whooping-cough were inconclusive. More experience is needed of *acute* lung infections due to penicillin-resistant organisms.

Intestinal-Tract Infections.—Forty-two cases of infantile diarrhoea have been treated by oral administration of 2-4 g. of streptomycin spread over seven days. Sensitive organisms rapidly disappear from the gut. As the infecting agent in this condition is not always the same it was to be expected that the results obtained in different centres would vary. Some centres report clinical benefit, but so far treatment has not been sufficiently controlled to warrant any definite conclusions. Further trials, in which streptomycin will be given to alternate cases, are being undertaken. A small number of cases of ulcerative colitis and of typhoid fever have been treated by oral and intramuscular administration with negative results.

Summary

In this series of cases streptomycin has often been successful in controlling the following infections : (1) Meningitis : *H. influenzae, Bact. coli, Ps. pyocyanea, Proteus,* and *Staph. pyogenes.* (2) Septicaemia : *Bact. coli* and *Ps. pyocyanea.* (3) Urinary tract infection : *Bact. coli, Proteus, Ps. pyocyanea, Str. faecalis,* and *Staph. pyogenes.* (4) Local sepsis: *Bact. coli, Proteus, Ps. pyocyanea, Staph. pyogenes,* and haemolytic streptococcus.

There have, however, been examples of almost every type of infection in which the micro-organisms rapidly became resistant. Courses of treatment should therefore be planned to exert the greatest possible influence from the beginning. The effect of combining streptomycin with other agents, such as the sulphonamides, is under investigation.

Owing to the short periods of administration toxic symptoms have been unusual and of slight importance. Urticarial rashes and skin irritation at the site of local application have occasionally been noted.

"C.B.11": A NEW ANALGESIC DRUG

PRELIMINARY COMMUNICATION

BY

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AND

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In experimental studies in human beings we have recently compared the pain-relieving properties of C.B.11 (4 : 4-diphenyl-6-morpho-linoheptan-3-one hydrochloride), pethidine, and physeptone (amidone). The method we used is a modification of that employed by Hewer and Keele (1947) in comparing the analgesic properties of physeptone, pethidine, and morphine. These authors, using a degree of ischaemic pain as their standard, found that the effects produced by 7.5 mg. of physeptone and morphine were equivalent to those of 75 mg. of pethidine. Because C.B.11 has been shown in recent studies (G. F. Somers, personal communication, 1947) to be a more effective analgesic than morphine in rats and of low toxicity we considered it was worthy of clinical trial in man.

Method

Ten volunteer medical students were trained to appreciate a degree of ischaemic pain produced by obstructing the blood flow to the arm by a sphygmomanometer cuff at a constant pressure of 220 mm. Hg. Following occlusion the subject contracted the flexor muscles of the forearm 60 times within the space of one minute. Contractions were then stopped and the ischaemia maintained, resulting in the development of a steadily increasing pain in the forearm. The degree of pain produced in five minutes was easily recognizable, and if the ischaemia was maintained it became intolerable in 10 to 15 minutes. The subjects were trained to recognize the level of pain reached in five minutes.

An intravenous injection of one of the three drugs under trial was then given into the opposite arm. On three separate occasions 5 mg. of C.B.11, 5 mg. of physeptone, or 50 mg. of pethidine was given, the order of injection being varied in different subjects. The analgesic effect of the drugs was estimated as follows: the degree of pain at the time of injection was tabulated as 100% ; an appreciable reduction of pain as 50% ; and reduction to a barely perceptible level as 20%. Records of the degree of pain experienced were made every minute until the pain again increased above the original level or it was evident that the quantity of drug given had not produced any analgesic effect. The results of the experiment are given in Table I.

TABLE I

	Pethidine 50 mg.	C.B. 11 5 mg.	Physeptone 5 mg.
Pain reduction to 20% ..	—	8	3
Pain reduction to 50% ..	—	1	3
No pain reduction	10	1	4

Discussion of Results.—In each case in which analgesia was produced the effect was apparent within two minutes and lasted as long with C.B.11 as with physeptone, the average duration being three minutes. After that period there was a rapid recrudescence of pain to above the original level with both drugs.

Side-effects.—With C.B.11 the injection was followed by transient dizziness, which did not last for more than five

minutes. Dizziness was slight or absent with physeptone or pethidine. With all three drugs there was a pleasant feeling of detachment, and with pethidine euphoria was marked in the majority of cases even though no relief of pain was noted. C.B.11 produced pupillary contraction in all 10 cases.

Clinical Study.—Eighteen patients suffering from pain of different types and of different degrees of severity were given C.B.11 in doses varying between 10 and 30 mg. The oral, intramuscular, and intravenous routes were all employed at different times. The results are summarized in Table II.

TABLE II

	No. of Cases	Complete Relief	Some Relief	No Relief
Coronary thrombosis	4	4	—	—
Teeth extraction	1	1	—	—
Pulmonary infarct	1	1	—	—
Pleurisy	2	2	—	—
Angina decubitus	2	—	1	1
Biliary colic	1	—	1	—
Gangrene	1	—	—	1
Sciatica	3	1	2	—
Neoplasm—secondary deposits	2	2	—	—
Miscarriage	1	1	—	—
	18	12	4	2

Given by mouth, 20 mg. of the drug produced analgesia in 20 to 30 minutes when the pain was not severe, the effect lasting for three to four hours. When the pain was more severe, as in cases of coronary thrombosis, a dose of 30–50 mg. was required to relieve the pain. No hypnotic effects were evident when the drug was given orally.

The intramuscular injection of C.B.11 produced relief of pain in 10 to 15 minutes—an effect which lasted two to three hours. Very little cortical depressant action was evident. The dosage used was 10–20 mg. Giddiness and vomiting were noted only in ambulant patients and not in those confined to bed.

Given intravenously in doses of 10–20 mg., analgesia was produced within two minutes and was accompanied by a feeling of dizziness, which passed off in a short time. The analgesic effect lasted for one to two hours.

Conclusion

This preliminary study suggests that C.B.11 is a potent analgesic, comparing favourably with physeptone, and is apparently more active than pethidine under the conditions of the experiment. In a short clinical trial it proved to be effective in the relief of some types of pain.

There is no evidence at present that C.B.11 is a drug of addiction.

We consider it is worthy of more extensive trial.

This study was suggested by Professor D. M. Dunlop, to whom we are grateful for advice and criticism. We are also grateful to Dr. H. M. Walker, of Glaxo Laboratories, for reports of the animal experiments and for supplies of C.B.11.

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The delegates to the first World Health Assembly will have "five weeks of very hard work," according to Dr. Brock Chisholm, Executive Secretary of the Interim Commission, who points out that "for the newly formed W.H.O., the member nations, and the secretariat there will be a year of hard work in 1949 to implement the decisions of the Assembly. As for the peoples of the world there is just beginning a realization of the W.H.O. constitution, which stands 'for the enjoyment of the highest available standard of health for every human being without distinction of race, religion, political belief, economical or social condition.'"

ASPHYXIA OF THE NEWBORN TREATED BY ROCKING

BY

F. C. EVE, M.D., F.R.C.P.

AND

The Late N. C. FORSYTH, M.D.

The unexpected death of Dr. Forsyth in November, 1947, lays on me the duty of publishing his work, which he was about to do. At Malton (Yorks) he had a large practice in midwifery of about 90 cases a year. Since 1932, when I published my rocking method of artificial respiration, he applied it to all his cases of "white asphyxia"—11 cases without a death. Hence his experience is unique and notable.

In 1947 I reported the case of a drowned boy of 14 treated (manually) by rocking (Eve, 1947). He was beyond recovery, but the colour change in his cheeks from blue to pink showed that an oxygenated artificial circulation had been created and maintained. I was excited to hear from Dr. Forsyth that the same colour change had occurred in all his 11 cases *before* the first gasp. I interpreted this to mean that rocking had restored a circulation to the respiratory nerve cells, which *then* were revived enough to make the respiratory muscles gasp. The lungs, unexpanded at first, may supply only a modicum of oxygen, but apparently that is enough for the modest demands of the nerve cells provided their blood is renewed by a *circulation*; stagnation is quickly fatal, and is aggravated by accumulated CO_2. Those with "white asphyxia" suffer from the enfeebled circulation of shock. Hitherto our conscious goal has been pulmonary ventilation. The first lesson learnt from these 11 cases is that we must concentrate on providing an oxygenated circulation (indicated by a pink face) to the nerve cells. If these are still viable they will then produce respiration in the natural manner. *Restore the circulation and the respiration restores itself.* The infant's heart can survive much longer, and rocking forces blood through the heart muscle.

Schmidt *et al.* (1945) were experimenting on the "gaseous metabolism of monkeys' brains." Finally the animals were killed by letting them bleed through the catheters which had been tied in the jugular veins. When heart and respiration had ceased they found (by chance) that by sucking out more blood from the jugular veins by a syringe "respiratory activity could be restarted and maintained for some time. This was confirmed by subsequent similar experiments, provided the monkey was in good condition." Hence they suggest that prompt manual artificial respiration may revive electric-shock patients by creating movement of blood in the cerebral vessels.

This recent evidence strengthens my plea that in asphyxiated babies natural respiration may be started by rocking if the cerebral blood (stagnant in quiescence) can be moved onwards. The valves in the heart ensure that the movement will be towards the heart. It is rarely remembered that every millilitre of venous blood which can be coaxed from the rigid cranial cavity is inevitably (I think) replaced by a millilitre of arterial blood from the lungs.

The second new and important lesson learnt from these 11 successful cases is that rocking is certainly not harmful in shock, and appears to be beneficial. The treatment at present orthodox in these asphyxia cases is concentrated on shock, and consists mainly of quiescence and hope. If rocking is harmless in shock it seems to me far preferable to this stagnation treatment.

Many of the dogs used in the rocking experiments of Hemingway and Neil (1944) had their upper spinal cord cut and had the low blood pressure of "spinal shock." Yet rocking maintained their circulation and was more effective than Schäfer's method or respiration by pump as regards oxygen consumption in the body. Schäfer's compression method could not be expected to expand the solid lungs of the newborn infant: they need expansion before they can be compressed.

Eight of Dr. Forsyth's cases were due to strangulation of the cord round the neck (nerve cells starved and anoxic); five were instrumental deliveries. He did not rock the few cases of cerebral haemorrhage which were born dead or died after a few gasps. Two recent cases were: (1) A breech case, born in white asphyxia with a faintly beating heart. The face turned pink after four or five double rocks, but the first respirations occurred only after rocking for eight minutes. (2) In a boy delivered by caesarean section the heart was impalpable. The first breath occurred after rocking for seven minutes, but the change in colour from white to pink was noted some minutes *before* the first gasp. This illuminating precedence (circulation *before* respiration) was observed by Dr. Forsyth in all his 11 cases. Has anyone observed it without rocking? I cannot get an answer. No one need be deterred from rocking by fear that it may increase a cerebral haemorrhage: the harm has already been done and the infant will soon be dead or better dead.

Dr. Forsyth's method in his first case was to rock the baby in his large hands before the fire (success after 35 minutes). Later he found it better to stand holding the baby, wrapped in a towel and lying on its side, to his chest. Thus he could hear the respirations, and the nurse could suck mucus from the throat with a No. 10 rubber catheter. He could rock the baby—as women do—by swaying his body through some 40 to 70 degrees each way without fatigue. I have verified these angles and find them easily attained if the knees are bent a little alternately. Gravity would have longer columns of blood to act on if the infant's legs were extended and the arms raised straight overhead. Ten double rocks a minute are enough. Presumably steep angles are best.

For clarity, I have so far deferred the CO_2 factor. In an important paper by Comroe and Dripps (1946) two adults with severe cerebral injury were investigated carefully. They survived about five hours without breathing or consciousness. Shock had reduced their blood pressure to 40–70 mm. Hg. Hence their condition resembled cases of newborn asphyxia: the colour was not recorded. They were kept alive by infusions and intratracheal oxygen for two to three hours, which oxygenated their blood (fully at first) and gave them a pink colour. Yet their arterial blood was found by analysis to be poisoned by CO_2 (tension 314 mm. Hg, equivalent to 44% alveolar CO_2), which did not betray itself to the clinician. This great excess of CO_2 would narcotize the nerve cells, depressing respiration and blood pressure. It could be washed out only by expansion and contraction of the lungs. Schäfer's method was tried, but it yielded only the "completely inadequate" tidal air of 72 to 117 c.cm., owing to lack of tonus in elastic recoil. Thus "the method fails when it is most needed—in deep asphyxia which abolishes tonus. On the other hand, Eve's rocking method gave the adequate tidal air of 286 to 500 c.cm., as it is independent of tonus. Circulatory benefits could not be measured."

From this paper we learn that our cases of newborn asphyxia are presumably being poisoned by excess of CO_2 until the lungs work. (This could be verified by blood analysis promptly after death in cerebral haemorrhage cases.) Also we do not know whether rocking expands the lungs effectively. (This could be ascertained by *x*-ray examination or at necropsy in cases of failure.) Meanwhile it seems reasonable to spend a few seconds in gentle mouth-to-mouth inflation of the lungs. *Then* we could confidently expect rocking to oxygenate the lungs and blood, sweep out excess of CO_2, and provide a circulation for the brain and heart muscle. Oxygen can be added, often with advantage. But to add 7% CO_2 to a probable 44% excess is deplorable poisoning.

I believe a co-ordinated research on some such lines would save many future citizens and much maternal anguish. I have tried in vain to compare Dr. Forsyth's results with those obtained in hospitals by other methods. There seems a deplorable lack of co-ordinate study in these awkward emergency cases. In the U.S.A., where 30,000 babies die annually of asphyxia, Dr. P. F. Flagg, chairman of the Asphyxia Committee of the American Medical Association, makes the same lament.

Some of my conclusions must be tentative until Dr. Forsyth's evidence is properly confirmed—notably, that if rocking restores the circulation the respiration restores itself.

My thanks for help are due to Professor A. Hemingway, Professor Alan Moncrieff, and Dr. Doreen Daley.

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GYNATRESIA: REPORT OF THREE UNCOMMON CLINICAL TYPES

BY

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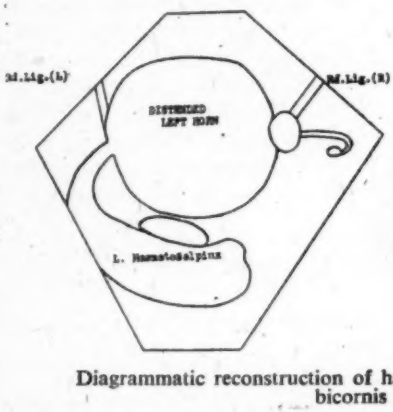
Anomalies due to aplasia of the female genital tract are not infrequent and, depending on the extent and location of the aplasia, all varieties and degrees of gynatresia may result. The more complex congenital abnormalities are usually associated with a non-functioning uterus and are rarely of much practical importance. I have recently had under my care three unusual types of gynatresia, with certain features in common. Failure of canalization was limited in extent and localized to the cervical or vaginal segments of the Müllerian tract, and the symptomatology was dependent upon the presence of a functioning uterus. Two were examples of haematometra due to atresia at the level of the cervix, and the third was a case of hydrocolpos, a condition in which an accumulation of watery or mucoid fluid in the vagina may produce serious mechanical effects during infancy and childhood.

Congenital Atresia of the Cervix with Haematometra

Case Report.—A married woman, aged 31, attended the Cardiff Royal Infirmary in September, 1945, complaining of right-sided abdominal pain. The pain had come on in attacks at irregular intervals for the previous twelve months, and these were increasing in severity. She had never menstruated. On speculum examination the portio and external os had a normal appearance, but the cervical canal was represented by a shallow blind depression, and the uterus was enlarged to the size of a three-months pregnancy. At laparotomy the uterus was found uniformly enlarged, and there was some distension of the

Fallopian tubes with blood. A longitudinal incision in the anterior uterine wall released about 4 oz. (114 ml.) of old menstrual blood, and the uterine cavity was found to end below in a blind pouch at the level of the isthmus. After separation of the bladder the anterior surface of the cervix was exposed and the vagina opened. A column of tissue, 2 cm. in length, which intervened between the external os and the uterine cavity was excised and a new canal fashioned over an indwelling catheter. Three weeks later the cervical canal was easily dilatable to No. 8 Hegar, and two years after the operation the patient was menstruating regularly, she was free from pain, and the uterus was normal in size.

Haematometra is most commonly caused by occlusion of the lower end of the vagina, and it then occurs as a secondary though important complication of haematocolpos. Stagnation of blood in the uterine cavity, due to obstruction at the cervical level, is usually an acquired condition and develops as a result of scarring following operation or childbirth. Haematometra due to strictures of obstetric origin generally occurs after difficult confinements associated with infection and much cicatrization (Padovani and Vuillième, 1931; Bernstein and Walter, 1939; Tait, 1945; Allen, 1947). Post-operative haematometra have usually been recorded after plastic operations on the cervix (Bernstein and Walter, 1939), but they have also occurred following the use of radium for benign uterine haemorrhage (Herring, 1939). In many cases of acquired stricture the stenosis is incomplete and, while blood accumulates within the uterus, there is some leakage past the obstruction. As a rule the distension by blood involves the entire uterine cavity, but Lifvendal (1933) has described a post-operative stricture of the cervix in which the haematometra was confined to the cervical canal. Retention of the menses is a quite unusual complication of carcinoma of the cervix, as this disease rarely causes stenosis of the cervical canal during menstrual life (Maliphant, 1939). Malignant occlusion of the cervix is predominantly a post-menopausal phenomenon, and pyometra is the common sequel. Most of the recorded cases of haematometra due to acquired stenosis of the cervix have required treatment by hysterectomy.

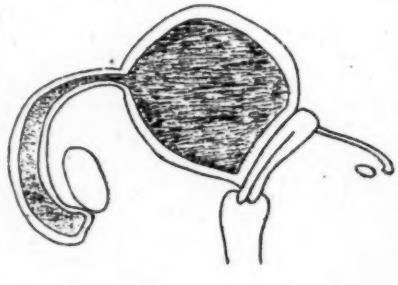


Diagrammatic reconstruction of haematoma of blind horn of uterus bicornis unicollis

Congenital occlusion of the cervix is a condition of great rarity, and few examples have been recorded in the literature. Cervical aplasia is usually associated with more complex developmental anomalies of the genital tract, and the uterus is then rarely developed enough to perform the function of menstruation (Bonney and McIndoe, 1944). Bernstein and Walter (1939) described 10 cases of haematometra of congenital origin, but they were all secondary to haematocolpos. Similarly, in Simon's (1928) series from the Mayo Clinic there was not a case of haematometra due to cervical atresia in an otherwise normal genital tract, but two recorded examples of this condition have been noted in the literature. Napoleao (1931) described congenital atresia of the cervix in a woman aged 37 who had complained of attacks of abdominal pain since the age of 15. There was a hypogastric swelling equal in size to a five-months pregnancy. The vagina was normal, the cervix nulliparous, and the cervical canal was obstructed by a septum at the level of the isthmus. When this was snipped half a litre of dark menstrual blood escaped. Monjardino (1936) also reports a case—in a young woman of 18—in which there was an imperforate septum across the cervix, and supravaginal hysterectomy was performed.

Haematometra in Atresic Horn of Uterus Bicornis Unicollis

Case Report.—A girl, aged 13, was brought to the Cardiff Royal Infirmary in September, 1947, on account of severe dysmenorrhoea. Her menses had started nine months previously, and were regular, lasting 7 days every 28 days. The menstrual pain was mainly localized to the left iliac fossa, but also extended to the buttock and to the left leg. For the past month she had also complained of dysuria and pain on defaecation. The girl was well developed and in good condition. On examining the abdomen a circumscribed spherical swelling was evident rising from the left side of the pelvis. Rectal examination showed that this was the upper pole of a mass which filled the left half of the pelvic cavity. The cervix was normal, and the uterus could not be distinguished apart from the main swelling. The provisional diagnosis was endometrioma.



On opening the abdomen free blood was found in the peritoneal cavity, and the pelvic organs had the appearance shown in the Diagrams. From the attachments of the round ligaments it was evident that the "tumour" was the distended left horn of a bicornuate uterus. It was about the size of a large orange. The right horn and corresponding appendages were normal, and were pressed against the right wall of the pelvis. Blood from the distended horn had been forced into the Fallopian tube to form a haematosalpinx, and blood had leaked into the peritoneal cavity. The left ovary was enlarged by oedema. On incising the distended uterine horn about 1/2 pint (284 ml.) of dark menstrual blood was released. No communication could be made out between this horn and the cervical canal, so it was excised together with the haematosalpinx. Convalescence was smooth, and menstruation has since been normal and painless. Histological examination of the blind horn showed typical uterine structure. Its endometrium showed hyperplasia with secretory changes.

Uterus bicornis is often symptomless and may be found accidentally in the course of an abdominal operation for some other condition. When one horn is atresic and fails to communicate with the cervical canal it may be the site of an ectopic pregnancy, but it is unusual for its endometrium to undergo menstrual changes. When this happens it is responsible for many diagnostic problems. Menstruation occurs normally from one half of the uterus, with the coincident development of a haematometra on the opposite side, and the condition is characterized by dysmenorrhoea of increasing severity. The dilated horn has usually been mistaken for a neoplasm, and the true state of affairs has become apparent only at operation. Even then, unless the relation of the round ligament to the swelling is noted, it may be mistaken for a blood cyst of the broad ligament. Wilson's (1925) case was that of a girl aged 14 who had menstruated four times and complained of severe dysmenorrhoea. As the nature of the condition was in doubt the uterus and adnexae were removed. Barris (1924) has described the condition in a woman aged 20, with a history of dysmenorrhoea for 18 months. Bernstein and Walter's (1939) case was that of a 27-year-old nulligravida, in whom the pre-operative diagnosis was fibroid uterus with ovarian

cyst. Simon (1928) reported unilateral haematometra in an incomplete uterus didelphys in a girl aged 17 who had complained of severe dysmenorrhoea for four years. These three cases were treated conservatively by resection of the atresic horn.

This form of uterus bicornis asymmetricus, although encountered infrequently, is a condition of some clinical importance. The stagnation of blood in the blind horn produces a characteristic clinical picture, and although the findings on palpation are often indefinite the history of intense dysmenorrhoeic pain so soon after puberty should make possible the correct diagnosis and appropriate conservative treatment.

Hydrocolpos

Case Report.—A girl, aged 14, was admitted to the Cardiff Royal Infirmary in March, 1944, with acute retention of urine. There was a suprapubic swelling, which partly disappeared on catheterization. The vagina was occluded by a retrohymeneal membrane, and it was evident on rectal examination that it was distended with fluid. The case was regarded as one of cryptomenorrhoea with haematocolpos, but on excising the membrane, which was unusually thick, about 1½ pints (850 ml.) of turbid watery fluid were released. The uterus and appendages were normal. The fluid contained many epithelial cells, and its protein content was 0.6%. It did not contain any fat globules, and was sterile on culture. Normal menstrual periods began five months after the operation and have continued normally since.

Congenital occlusion of the lower end of the vagina is not an uncommon condition, but it is rarely responsible for symptoms before puberty. The object of this report is to draw attention to a clinical entity characterized by the retention in the vagina of enough watery or mucinous fluid to produce symptoms in infancy and childhood. In the literature the condition has been described as "hydrocolpos" or "mucocolpos," and the fluid as "turbid serous," "milky," or "mucinous" in character. The retained fluid, which is regarded as the accumulated secretions of the cervical and uterine glands, contains desquamated epithelial cells with some leucocytes, and is sterile on culture. A variable amount of mucoid vaginal discharge is not uncommon in the newborn, and it is probable that in most cases of vaginal atresia there is some accumulation of uterine secretions, but not in sufficient quantity to produce symptoms until augmented at puberty by the products of menstruation. The large accumulations of sanguineous fluid in some cases of cryptomenorrhoea after one or two attacks of abdominal cramps may represent cases of pre-existent hydrocolpos into which the first few menstrual bleedings have flowed. When abnormal activity of the uterine glands coexists with vaginal occlusion such a collection of fluid may form in the genital tract that serious effects may be produced long before the onset of menstruation.

Summary of the salient features of the recorded cases of hydrocolpos and hydrometrocolpos

Age	Clinical Features	
In infancy: 1 day	Found at necropsy in a baby with imperforate anus and intestinal obstruction. 1 oz. (28 ml.) of light yellowish mucoid material in vagina	Mahoney and Chamberlain (1940)
2 days	Large abdominal tumour. Several ounces of turbid fluid released per vaginam	" "
17 "	Progressive abdominal enlargement with retention of urine. Several ounces of mucinous grey fluid released p.v.	Rosenblatt and Woolley (1943)
3 weeks	Large abdominal tumour with retention of urine. Large amount of turbid mucoid fluid released during panhysterectomy	Mahoney and Chamberlain (1940)
7 "	Retention of urine, intestinal obstruction, and oedema of legs. Laparotomy followed by incision of hymen	Morris (1945)
8 "	Retention of urine, abdominal swelling and diarrhoea. Laparotomy followed by incision of hymen and release of 2 oz. (56 ml.) of milky fluid	Mahoney and Chamberlain (1940)
8½ "	Retention of urine, abdominal tumour, vomiting, and diarrhoea. Laparotomy followed by incision of hymen and release of 2 oz. of milky fluid	Kereszturi (1940)
11 "	Cystic swelling at vulva. 1 dr. of mucus released p.v.	Spencer (1916)
Pre-pubertal group:		
12 years	Abdominal swelling. Two quarts (2·27 litres) of milky chyle-like fluid released per vaginam. Menstruated 5 months later	Bowen (1941)
14 "	Abdominal swelling and backache. Laparotomy and 2,200 ml. of serous fluid removed by puncture of "pelvic cyst"	Althoff (1941)
14 "	Abdominal swelling with retention of urine. 1½ pints (850 ml.) of turbid watery fluid released per vaginam. Menstruated 5 months later	Maliphant (1948)

The cause of the abnormally copious secretion of fluid is obscure, but it is probably related to the activity of the uterine glands, and this is controlled by the oestrogenic hormone. The foetus *in utero* is exposed to the influence of maternal oestrogens, and also, according to Dobszay (1938), for the first two weeks after birth. The oestrogens of maternal origin are responsible for the vaginal discharge often observed in newborn infants, and also for the transient uterine bleeding and breast enlargement which may occur. During this phase there is histological evidence of increased activity of the uterine and cervical glands, and the vaginal epithelium resembles the adult type. The vaginal epithelium of adults and of infants during the first few weeks of life contains glycogen, but this is not found in the vaginal epithelium of older children before the age of puberty (Dobszay, 1938). When the infant is about 2 weeks old this change occurs in the character of the vaginal epithelium, and the uterine glands become less active in appearance (Mahoney and Chamberlain, 1940).

The morbid histology of hydrocolpos in infancy has been described in operation and necropsy specimens by Mahoney and Chamberlain (1940). They found distinct evidence of activity of the uterine glands and varying degrees of keratinization of the vaginal epithelium. The great variation in the amount of uterine secretion is considered by them to be dependent upon the degree of oestrogen stimulation, and if this view is correct increased glandular activity would be expected to occur during foetal and early neonatal life, and again shortly before puberty. It is noteworthy that most of the recorded cases of hydrocolpos fall into one or other of these two age groups. The first category includes infants who either are born with enormous collections of secretion in the vagina or have accumulated such secretions during the first few weeks of life. The second category is comprised of cases in which symptoms of fluid distension of the vagina develop shortly before puberty, when there is awakening activity of the uterine glands.

The mechanical effects of distension of the vagina are well recognized. The vagina is capable of enormous distension even in infancy, and will accommodate a large collection of fluid before the uterus is affected. In this phase the uterus is merely displaced upwards and rides on the greatly distended vagina as a small nodule. When the intravaginal fluid pressure is sufficiently increased haematometra or hydrometra follows, with reflux into the Fallopian tubes. The distension of the vagina also causes upward displacement of the bladder and stretching of the urethra and bladder neck, so the commonest initial symptom in both haematocolpos and hydrocolpos is retention of urine. Other pressure effects in infancy, such as intestinal obstruction and oedema of the lower extremities, have been described (Morris, 1945).

Hydrocolpos in Infancy

It is during the first two months of life that hydrocolpos has its most serious consequences. The literature of the

condition was reviewed in 1940 by Mahoney and Chamberlain, and cases have since been reported by Kereszturi (1940), Rosenblatt and Woolley (1943), and Morris (1945). It is one of the causes of large cystic abdominal swellings in female infants, and the rational and only treatment required is excision of the occluding membrane. However, without inspection of the vulva and rectal examination the true pathology is apt to be overlooked, and laparotomy with its attendant dangers in a young infant may inadvertently be employed.

The infant is distressed, and progressive abdominal enlargement and retention of urine are usually conspicuous symptoms. The main abdominal swelling is distended bladder, and after catheterization a much smaller second swelling is noted in the lower abdomen. The vagina is occluded by a bluish membrane which bulges when the child strains, and rectal examination reveals fluctuant distension of the vagina. Mahoney and Chamberlain have drawn attention to the diagnostic value of injecting radio-opaque substances through the point of atresia, and Rosenblatt and Woolley confirm the value of roentgenoscopy in establishing a correct diagnosis.

Hydrocolpos may cause alarming symptoms two days after birth (Mahoney and Chamberlain, 1940), and cases have been recorded in infants of 17 days (Rosenblatt and Woolley, 1943), 7 weeks (Morris, 1945), and 8½ weeks (Kereszturi, 1940). Morris's case of hydrometrocolpos was complicated by hydronephrosis, intestinal obstruction, and oedema of the lower half of the body. An instructive case was reported by Kereszturi in an infant of 8½ weeks. The imperforate condition of the hymen was noted, but was not considered to be of clinical significance. A barium enema showed the colon to be displaced upwards, and intravenous urograms revealed bilateral hydronephrosis with obstruction of the ureters at the uretero-vesical junction. As the infant was losing ground and the diagnosis was "pelvic tumour of unknown origin" laparotomy was performed. A cystic tumour was found filling the pelvis and pushing the bladder upwards and forwards; pressure on this tumour caused bulging of the hymen. Before the abdomen was closed 2 oz. (56 ml.) of milky fluid was released from the vagina by incising the hymen, whereupon the pelvic tumour collapsed. In this case the hydrocolpos and hydronephrosis were complicated by pyelonephritis with severe constitutional symptoms, and the urograms did not return to normal for a period of 15 months.

Spencer (1916) has described mucocolpos in a baby girl, 11 weeks old, in which the condition was recognized before the onset of obstructive symptoms. The mother had noticed a swelling in the vulva which became a little more prominent when the baby cried. An elliptical piece of the imperforate hymen was excised and about 1 dr. (3.5 ml.) of mucus escaped. Spencer stressed the importance of examining as a routine the vulvae of female babies at birth. Unless this is done any vaginal occlusion usually escapes notice until menstruation occurs, and the genital tract may then receive irretrievable damage.

Hydrocolpos in Girls shortly before Puberty

Records of two cases of this type were found in the literature and I have now added a third. The clinical features are indistinguishable from those of haematocolpos, although the absence of monthly twinges of abdominal pain may be significant.

Bowen's (1941) case was that of a girl aged 12 who complained of lower abdominal discomfort and had a soft symmetrical mass extending from the symphysis to the umbilicus. Incision of the vaginal septum released 4 pints (2.27 litres) of milky chyle-like fluid. The girl menstruated five months later. In Althoff's (1941) case, quoted by Morris, a 14-year-old girl complained of abdominal pain and backache for six weeks. The hymen was imperforate, and when it was punctured 50 ml. of cloudy serous fluid was withdrawn. As the nature of the condition was still in doubt the abdomen was opened and 2,200 ml. of the same type of fluid was obtained by aspiration of a large cyst-like structure which arose from the pelvis.

Summary

Three types of gynatresia are described. They each had distinctive clinical features and were amenable to conservative treatment. Developmental anomalies of this order, though rare, are of much practical interest, for unless recognized they may be submitted to needlessly radical operative procedure.

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Medical Memoranda

Acute Purpura with Neurological Complications Associated with "Sedormid" Therapy

The following case report seems to be interesting enough to merit publication.

CASE HISTORY

The patient, a woman aged 30, had been admitted to the Bristol Royal Infirmary three months previously for a thyroidectomy, and after her discharge had been given "sedormid" by her doctor. She had taken about 14 tablets at very irregular intervals in the course of two months. Three days before admission she had noticed a purpuric rash on her arms and legs, and on the day of admission she had had haematemesis, haematuria, and melaena.

On examination a widespread purpuric rash was seen; but the spleen was not palpable and there was no enlargement of the peripheral lymph glands. Macroscopic haematuria was present. A blood count showed: red cells, 3,000,000; haemoglobin, 56%; white cells, 3,600, with normal differential count. Bleeding time was 26½ minutes; clotting time, 8½ minutes; clot retraction was very poor. Only one platelet was seen in the whole film and no estimate of their number could be made.

The next day, after a transfusion of 2 pints (1.14 litres) of fresh blood, there appeared a right-sided facial palsy of lower motor neurone type. On the following day dissociated anaesthesia (loss of pain and temperature, normal to cotton-wool) developed on the right side of the face, greater in the first and second division of the trigeminal nerve than in the third. No other abnormal physical signs were elicited, except for the right facial palsy previously noted, but the patient complained of a severe occipital headache and neck stiffness. Three days later she had had no further haemorrhages and her bleeding time was now 8½ minutes, although the platelets were still too few to make an accurate count. Her progress afterwards was uneventful, and on discharge 10 days later the platelets had risen to normal, and her bleeding time was now 4 minutes.

Nine days later she was readmitted, having had a further haematemesis and massive purpura; no platelets were seen in her blood. During the next 13 days she received 11 pints (6.25 litres) of blood —5 pints (2.84 litres) being fresh blood—and at the end of this time the platelets had risen to 3,000 per c.mm. and the haemoglobin

was 90%. Her condition appeared to be satisfactory for three days, but purpura developed once again and she suddenly went into coma the same night and died.

A post-mortem examination was performed by Dr. R. G. Sandry. There were numerous petechial haemorrhages in the skin. Many small haemorrhages were also seen beneath the parietal and visceral peritoneum and pleurae, and beneath the epicardium. The spleen was enlarged to about twice its normal size and the pulp was somewhat softened. Histologically it showed no noteworthy change. The lymph nodes were slightly enlarged and purple in colour. Histologically it was evident that all the glands examined had been draining areas of haemorrhage. The bone marrow of the sternum was abundant and red, containing one area of haemorrhage. There was extension of red marrow down the shaft of the femur. Histologically, specimens of marrow taken from the sternum and from the mid-shaft of the femur were virtually indistinguishable. In both there was some hyperplasia of the erythroid series of cells. Megakaryocytes, although present, were relatively few in all sections examined. The left cerebral hemisphere was the seat of a massive haemorrhage, this being the ultimate cause of death. No haemorrhage, recent or old, could be found in the region of the descending nucleus of the fifth cranial nerve.

DISCUSSION

The first case of purpura due to sedormid (allylisopropylacetylurea) was published by Dening (1933); since then a number of cases have been reported in the literature. An interesting feature of my case was the accidental discovery of a positive Hess test in the patient's sister whilst using her as a fresh blood donor: no abnormality in her bleeding time or platelets was discovered, but it is suggested that there was some familial capillary abnormality in this case, and that sedormid therapy finally produced a further change in platelet production. A fatal relapse of purpura occurring nine days after discharge from hospital without further sedormid therapy is unusual, but it is suggested that the marrow, as evidenced by paucity of megakaryocytes, had been affected by the therapy.

Various therapeutic measures were tried, including blood transfusion, 5 ml. of intramuscular liver, vitamins C, P, and K, and 120 mg. of rutin daily. Rutin, an extract of buckwheat, is stated to have an effect on capillary permeability, but in this case it appeared to have little effect.

I wish to thank Dr. Orr-Ewing for permission to publish this case report, and Dr. Sandry, of the Pathological Department, University of Bristol, for the post-mortem findings.

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Instantaneous Traumatic Forequarter Amputation of the Right Arm

A search of the literature does not show any reference to traumatic forequarter amputation of the arm. Berman (1945) discusses operative interscapulothoracic disarticulation of the arm. It is considered, therefore, that this case may be worth placing on record.

CASE REPORT

The patient, a healthy miner aged 23, was freeing a coal-conveyor belt which had become clogged with coal at the roller end and had stopped. His right arm was through a hole in the protective grille. The moment the belt was free it began to move rapidly, and the patient's arm was caught between roller and belt and twisted round so that it was avulsed from the body.

On admission to the casualty department he was found to be shocked but not in a serious condition. After the wound had been rapidly inspected for a serious haemorrhage anti-shock therapy was begun, including 2 pints (1.14 litres) of blood and 2 pints of plasma. Two and a half hours later he was operated upon under thiopentone and gas-and-oxygen.

On examination the skin around the shoulder showed an aperture 6 in. (15 cm.) vertically by 3 in. (7.5 cm.) horizontally, with loose and undermined edges for varying distances anteriorly and posteriorly along the chest wall. There was also a flap of skin on the anterior edge which came from the upper arm. Deeper inspection showed that there was no scapula present, and that the lateral half of the clavicle was missing. There had been, in fact, a formal surgical forequarter amputation. It was difficult to insert the hand into the bed of the scapula.

The pectoral muscles had been torn through near their insertion, the serratus anterior could not be found except for a few slips on the ribs, the latissimus dorsi was quite intact, and only portions of the levator scapulae, rhomboids, and trapezius were found. The avulsed limb was unharmed. The axillary artery had been avulsed about 1½ in. (3.75 cm.) from the first rib; apparently there had been no serious haemorrhage at the time of the accident owing to the avulsion nature of the injury. The brachial plexus had been severed at about the same level as the vessels.

The axillary artery and vein were ligated at the outer border of the first rib. The brachial plexus was cut short and injected with 2% procaine. Haemostasis was then secured at other points. Complete closure was possible, utilizing the flap of skin on the anterior margin of the wound. A drain was passed up into the "axilla" and a coaptation suture was inserted to hold the sutured flaps to the chest wall. Throughout the whole operation the patient's condition remained excellent. Antitetanus and anti-gas-gangrene sera were given and a prophylactic course of penicillin was started.

Complete primary union was secured. The patient was in hospital for 14 days, during which time deep breathing exercises were encouraged. He complained of pain in his "phantom" limb for some time, and when this continued it was considered that the cause might be calcification in the region of the brachial plexus. A radiograph, however, showed complete absence of calcification. The nature of his "phantom" limb was peculiar; he complained that he could feel his hand and forearm but that they were attached to a very short upper arm. It may be noted that it was his hand and forearm which were primarily trapped in the machine.

I wish to thank Mr. L. E. Sutcliffe, surgeon-in-charge of the accident service, for permission to publish, Dr. H. E. Pooler for the administration of the anaesthetic, and the sisters and nurses of the casualty department and accident ward for their help and aftercare of the patient.

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REFERENCE

Berman, J. K. (1945). *Surgery*, **18**, 256.

A Case of Poisoning by Ethylene Trichloride

A boy aged 16 had been employed at a factory for two years where one of the principal jobs consisted in the degreasing of metals by means of ethylene trichloride. Notices to the effect that this substance was dangerous were posted throughout the factory, and the boy had been particularly warned of its danger.

The degreasing of large metal parts was accomplished in a large vat containing ethylene trichloride, but it was possible to draw off the liquid into a bucket by means of a tap at the bottom of the vat, and, indeed, small metal parts were generally cleaned by rinsing them in a bucket containing ethylene trichloride. The vat was accessible to anyone working in the factory. On one occasion a workmate had found the boy smelling the liquid with evident pleasure.

At about 4 o'clock one afternoon the boy was heard to say that he was shortly going home to tea, but an hour and forty minutes later he was found in a lavatory some 30 yards (27 metres) from the vat lying on the floor with his head over a bucket the bottom of which was covered to a depth of 2 in. (5 cm.) by ethylene trichloride. He was dead.

At necropsy he was found to be adequately nourished and healthy. Superficial burns, reminiscent of anaesthetic burns, were seen on the left side of the face. The sweet smell of ethylene trichloride was most pronounced in the brain, lungs, and stomach, and the chief pathological changes were seen in the respiratory tract, where there was acute inflammation of all the air passages and an intense haemorrhagic oedema of the lungs. A little regurgitated vomit was found in the trachea. The cause of death was given as acute pulmonary oedema following the inhalation of ethylene trichloride, and the circumstances left no doubt that the boy had been inhaling the fumes of ethylene trichloride because he liked either the smell or the sensation which they produced.

Addiction to ethylene trichloride is mentioned in the M.R.C. Report (No. 80) on the toxicity of industrial organic solvents.

The principal use of ethylene trichloride is as a degreasing agent, for which purpose it is used in the dry-cleaning industry as well as in the treatment of metals. As a solvent of tar and pitch it is sometimes found in certain paints, and it has a limited use as an insecticide.

DONALD TEARE, M.D., M.R.C.P.,

Reviews

MALARIA

Pathological Processes in Malaria and Blackwater Fever. By Brian Maegraith, M.A., D.Phil., B.Sc., M.B. (Pp. 430; illustrated. 35s.) Oxford: Blackwell Scientific Publications. 1948.

The relation between the clinical signs and symptoms of malaria and the pathological changes of the disease has long excited interest and investigation. More than 400 years ago Albert Dürer, it may be recalled, illustrated a letter to his physician by drawing a sketch of himself indicating his enlarged spleen and announcing, "That's where the pain is." The gross pathological lesions associated with malaria have long been recognized, but it is only during the last twenty years that improvements in technique have permitted an investigation of the biochemical lesions in malaria and a correlation of these lesions with the metabolic needs of the malarial parasites; information has thus been collected in a somewhat haphazard way. This book is the first attempt at a synthesis of the ascertained facts and as such it is an important achievement, not only because it sets out what is already known but perhaps even more because it reveals the very considerable lacunae still existing in our knowledge of malaria.

In the first chapter the author outlines the main clinical features of malaria; his account is designed more especially for those who may not be entirely familiar with the various forms of the disease in man. There follows a complete description of the morphology of malaria parasites by Dr. R. H. Black, who brings to the task the knowledge that he has acquired from studies of plasmodia in cultures. He also fully discusses the physiology of the parasites, as well as the morphological changes and metabolic derangements caused by various antimalarial drugs. This is a subject which requires much further investigation. Dr. Maegraith then considers the effects of malaria on the various organs of the body. Through some process which is not yet fully understood the red cells which are not actively invaded by parasites are nevertheless destroyed in considerable numbers at the time of the paroxysm. In infections due to *Plasmodium falciparum* the loss of red cells may be as high as 500,000 cells per c.mm. The author emphasizes the role of anoxia in the genesis of the lesions in the various organs, more especially in the liver and kidneys; in the genesis of derangements in the central nervous system the process of anoxia may be modified in some degree by hypoglycaemia. He concludes with a general summary of the pathological processes in malaria, such factors being considered as the still uncertain mechanism of the paroxysm, the role of haemozoin, and the tissue response to infection.

The author might have said more about the part played by humoral immunity as opposed to the phagocytic mechanism: the antithesis between latent infection and what is termed "a general humoral immunity" is not entirely clear. A few minor criticisms can be readily met in a second edition. The nomenclature of antimalarial drugs has not been satisfactorily worked out. The use of names which are official neither in Great Britain nor in America is to be deplored, as is the failure to spell consistently the names used. In the marshalling of so many references it is hardly surprising that there are occasional errors in ascribing priority, as for instance the failure to mention the pioneer work of E. K. Marshall and his colleagues (1942) on the action of *p*-aminobenzoic acid in inhibiting the antimalarial action of sulphonamides. Inclusion of an author index would improve the book.

However, it is an important and stimulating work which should be pondered over by all who are in any way associated with the problems of malaria; as there are on a conservative estimate some 700 million victims of malaria in the world, quite a number of people should undoubtedly study it. Not everyone will necessarily agree with all the views put forward, but some of the pundits may learn how tenuous is the evidence in favour of theories which have too long masqueraded as facts. Above all, this work emphasizes how great is the need for further investigation into the highly complex pathological processes which arise when once malarial plasmodia have entered the body.

G. M. FINDLAY.

CONSCIENCE

The Battle of the Conscience. A Psychiatric Study of the Inner Working of the Conscience. By Edmund Bergler, M.D. (Pp. 296. $3.75.) Washington: Washington Institute of Medicine, 1720, M. Street, N.W.

In the literature of psychiatry the tendency is to classify and relate mental breakdowns and to assign broad aetiological factors. While psycho-analytic writings on the other hand are confined to tracing the dynamic relations of mental development, unfolding this war of conflicting trends which give rise by repression and reaction formation to both neurosis and character, they leave the common medical reader with the impression that the person disappears in the analytic bombardment as atoms disappear into nuclear substance in the pile. It is a relief, therefore, to see in this volume actual persons not disappearing but illuminated under the fierce, cynical glare of the psycho-analytic spotlight.

While the author discusses a wide field of mental processes, he focuses his attention on the vital problem of conscience in its unconscious manifestations—the super-ego of theory which determines from an early age the deeper moral preoccupation that gives quality to character and intense suffering to the victim of mental disorder, particularly the anxiety states, the obsessions and depressions, and the torture of insomnia. He shows how much more imperative can be the dictates of this unconscious regulator of conduct and to what lengths the human being can go in meeting it by subterfuges of which he is not consciously aware. The book is amply supplied not only with case examples but with literary references and attempts at literary analysis not unfamiliar to us in psycho-analytic literature.

The author writes racily and shows a high competence in analysis as well as a freezing penetration of human nature. This makes his approach cynical and destructive, for in his exposition he sees the working of conscience in all mental attitudes; people appear to be left with only a shred of reality sense, and the ego seems to disappear between the nether millstone of instinctive urge and the upper stone of the super-ego. If this is the *reductio ad absurdum* of analysis, then culture has certainly reduced mankind to the state of conscience-ridden cowards and hypocrites. The besetting weakness of the book, otherwise both readable and instructive, is the excessively sensational style of the chapter headings—e.g., "The Injustice Collector"; "Success without Blessings of Conscience"; "Neurotics who Bargain for the Electric Chair."

EMANUEL MILLER.

TEXTBOOK OF MIDWIFERY

A Textbook of Midwifery for Students and Practitioners. By R. W. Johnstone, M.A., M.D., F.R.C.S.Ed., M.R.C.P.Ed., F.R.C.O.G., F.R.S.Ed. 13th edition. (Pp. 570; 307 illustrations. 30s. net.) London: Adam and Charles Black. 1948.

Professor Johnstone's *Textbook of Midwifery* will be familiar to many generations of medical students, for it is now 35 years since the first edition appeared. This new edition retains the well-known characteristics, and the general arrangement, including individual chapter headings, has hardly changed in the last 20 years at least. This does not imply that it has not kept abreast of the very considerable advances in the theory and practice of obstetrics in recent years, but rather that the book has always had a sound foundation. Indeed, the author is fully justified in claiming that he presents in this edition a thoroughly up-to-date account of what is generally accepted by the majority of modern obstetricians. The new features include a more detailed description of the maternal reactions to pregnancy, antenatal care, and diet during pregnancy and lactation. The chapter on disordered uterine action has been rewritten to give a much more reasonable account of a difficult subject than is usual in textbooks. The complete segregation of hyperemesis gravidarum from the toxaemias of pregnancy is in keeping with current thought. Dr. W. I. C. Morris has contributed a section on incompatible blood groups in relation to midwifery.

Apart from some inevitable differences of opinion over detail, this by and large is a most satisfying textbook. On reading it again after an interval of many years it is easy to understand why it has enjoyed such continued popularity with undergraduates and practitioners. In the first place the author has

succeeded in keeping pace with advancing knowledge, and in including some useful reference to almost every condition likely to be encountered in professional examinations or in practice, without increasing the size of the book to any great extent. Above all, however, the book is concise and methodical, easy to read and to understand, and contains views likely to meet with general acceptance rather than highly individualistic opinions. Some of the illustrations perhaps lag behind the high standard set by most modern books, but this again may appeal to the student, for it helps to keep the cost within reasonable limits.

T. N. A. JEFFCOATE.

USES OF STREPTOMYCIN

La Streptomycine et ses Applications Thérapeutiques (principalement dans la Tuberculose). By Prof. C Levaditi. (Pp. 218; 76 figures. 350 francs.) Paris: Presses Documentaires, 28, rue Saint-Dominique, VIIe. 1948.

The author of this book, the director of the Institut Alfred Fournier, France, assembles the knowledge of the laboratory aspects of streptomycin in a form useful for research workers and others. His aim also is to review the clinical applications of the antibiotic, particularly in tuberculosis, but in this he has been less successful, partly because of the rapidly changing picture given by clinical trials. Professor Levaditi and his colleagues have themselves been active in experimental work on streptomycin, and many of their results are given; they tend to confirm previous conclusions rather than to break new ground. The book can be recommended for its concise presentation.

P. D'ARCY HART.

HOSPITAL ADMINISTRATION

Problems of Hospital Administration. A Report on a study based upon interviews with 100 Hospital Administrators located in various sections of the United States. Charles E. Prall, Director Joint Commission on Education. (Pp. 104. No price given.) Chicago: Physicians' Record Company.

The profession of hospital administrator is a more distinct one in the U.S.A. than in Britain, and training courses have been established by many bodies, including universities. Those responsible for devising courses and curricula have realized that, until it is clearly understood what the functions of a hospital administrator are or ought to be, provision of adequate training to an approved standard is impossible.

A joint Commission of Education was set up by the College of Hospital Administrators and the American Hospital Association to make a wide survey of the field and to submit what would be in effect a careful job-analysis of the work of a hospital administrator. This book is the result of the investigations and is based largely on interviews with 100 leading administrators chosen because of their approved experience and efficiency, some being medical, some lay, and representative of all varieties of hospital, voluntary and State, large and small. Every aspect of hospital work is touched on, the questions and answers covering every conceivable problem both of policy and day-to-day running. The book is a useful record of facts, and on it the Commission of Education will base its recommendations for an optimum curriculum. This book and the Commission's recommendations should be of great value to all interested in hospital control and management in Britain.

ANDREW TOPPING.

Sir Alfred Pearce Gould's well-known manual, *Elements of Surgical Diagnosis*, ninth edition revised by Sir Cecil Wakeley (Cassell, 15s.), has reached the age of 63 years and is still popular—a fact that speaks well for its usefulness, for the law of survival of the fittest operates efficiently in the medical literary world. Sir Alfred was one of the best surgical teachers of his time, and on looking into this volume one can see the secret of his success, for here we find lucid exposition, clear differentiation of signs and symptoms, and definite direction leading to accurate conclusion. The last edition was by the original author's son, but Eric Pearce Gould unfortunately died during the recent war. Sir Cecil Wakeley has ably revised the text. He constantly used the book when a student and appreciates exactly what its function is in the education of the student. The revision was therefore (as he says in the preface) a labour of love, and he has preserved the excellent tradition of the book. We can cordially recommend it to the student and, for that matter, to the teacher of surgery.

BOOKS RECEIVED

[Review is not precluded by notice here of books recently received]

The Skull, Sinuses, and Mastoids. By B. R. Young, M.D (Pp. 328. 36s.) London: H. K. Lewis. 1948.

A handbook of *x*-ray diagnosis, with many skiagrams

The Medical Clinics of North America. Symposium on Psychiatry and Neurology. By various authors. (Pp. 555-853. No price.) London: Saunders. 1948.

A collection of clinical articles

Pharmacology. By J. H. Gaddum, Sc.D., F.R.S., M.R.C.S., L.R.C.P. 3rd ed. (Pp. 504. 25s.) London: Geoffrey Cumberlege. 1948.

New material is included on BAL, folic acid, anticoagulants, antibiotics, and other topics.

Petticoat Surgeon. By B. Van Hoosen. (Pp. 334. 12s. 6d.) London: Peter Davies. 1948.

The autobiography of a woman surgeon.

Laboratory Diagnosis of Protozoan Diseases. By C. Franklin Craig, M.D., M.A., D.Sc., F.A.C.S., F.A.C.P. 2nd. ed. (Pp. 384 27s. 6d.) London: Henry Kimpton. 1948.

A manual of laboratory methods.

Basic Principles of Ventilation and Heating. By T. Bedford, D.Sc., Ph.D. (Pp. 401. 25s.) London: H. K. Lewis 1948.

Ventilation and heating in terms of basic human needs

British Surgical Practice. Edited by Sir E. Rock Carling, F.R.C.S., F.R.C.P., and J. Paterson Ross, M.S., F.R.C.S. Vol. 3. (Pp. 524. 60s.) London: Butterworth. 1948.

Subjects continued alphabetically—from Caesarean Section to Eyelids.

Mental Abnormality. By M. Culpin, M.D., F.R.C.S. (Pp. 196. 7s. 6d.) London: Hutchinson. 1948.

An outline of the subject for the general public.

Glomerular Nephritis. By T. Addis, M.D., F.R.C.P. (Pp. 338. 40s.) London: Macmillan. 1948.

A description of the author's method of diagnosis and treatment

The Surgery of Abdominal Hernia. By G. B. Mair, M.D., F.R.F.P.S.G., F.R.C.S.Ed. (Pp. 408. 25s.) London: Edward Arnold. 1948.

A monograph concerned with the causes and treatment of abdominal herniae.

The New Science of Surgery. By F. G. Slaughter, M.D. (Pp. 241. 10s. 6d.) London: Sampson, Low, Marston 1948

A description of the triumphs of modern surgery for the layman.

Modern Surgery for Nurses. Edited by F. Wilson Harlow, M.B., B.S., F.R.C.S. (Pp. 795 25s.) London: Heinemann. 1948.

A textbook for nurses written by a number of specialists

Treatment in General Practice. By H. Beckman, M.D 6th ed. (Pp. 1,129 57s. 6d.) London: W. B. Saunders. 1948.

Therapeutics for the general practitioner.

Clinical Diagnosis by Laboratory Methods. By J. Campbell Todd, Ph.B., M.D., and A. Hawley Sanford, A.M., M.D. 11th ed. (Pp. 954. 37s. 6d.) London: W. B. Saunders. 1948.

A working manual of clinical pathology.

Diseases of the Skin By O. S. Ormsby, M.D., and H. Montgomery, M.D., M.S 7th ed. (Pp. 1,462 90s.) London: Henry Kimpton. 1948.

A new and revised edition of a textbook of dermatology.

Anatomy and Physiology Laboratory Manual and Study Guide. By B. Griffith King, Ph.D., and H. M. Roser, B.A., M.A. 3rd ed. (Pp. 267. 15s.) London: W. B Saunders 1948.

A guide for those who have to give practical instruction in anatomy and physiology to nurses.

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SAFETY IN CHEMICAL WORKS

The aim of those responsible for safety in factories is so to control the physical environment and so to stimulate the consciousness of workers that accidents are reduced to unpredictable events. Experience shows that most accidents could have been foreseen. Appropriate rules and regulations can be drawn up for the prevention of serious accidents, but compliance with the law alone will not necessarily reduce their incidence. The human factor, so hard to define and so real in the daily life of a factory, still dominates the picture. Were it possible so to operate industrial processes that the incalculability of man had no relevance to the problem of safety, then the incidence of accidents would fall sharply. The story of the manufacture of the atom bomb illustrates what can be achieved in spite of the extreme dangers involved. The concentration of effort on safety measures and the availability of means to implement them are still far from adequate in the general body of industry. Because of expense perfect environmental conditions cannot be provided, and reliance is placed on exhortation, propaganda, and training in safety. The response to this is improving but is still far from satisfactory.

In the chemical industry the opportunities for calamitous accident are many. Injuries, explosion, poisoning, and industrial disease menace the worker continually. In spite of technical conformity with the legal requirements the conditions in many chemical factories are bad. An almost traditional belief that the industry is necessarily a dirty one inhibits the efforts which are necessary to establish better practice. The workers who are employed in the industry are, in general, of the less developed type and correspondingly difficult to educate in co-operative safety measures. At the present time almost insuperable obstacles prevent even the best of managements from improving or renewing plant and from introducing those amenities which not only improve the self-respect of the worker but also are essential if safe working is to be attained.

Even in the chemical industry most accidents are not due to chemical faults but to falls, falling objects, moving machinery, tools, handling goods and articles without machinery, stumbling over obstructions, and the like. Probably not more than some 5–10% of all accidents in chemical factories are due to actual chemical products. This figure must, of course, be distinguished from the incidence of industrial diseases such as poisonings, dermatitis, tumours, and eye affections. It is obvious that in order to reduce accidents in chemical factories the rules of safety applicable in other types of industry must be no less earnestly applied: good housekeeping, clean working, good lighting, heating, and ventilation, effective guarding of machinery, and mechanical methods of lifting and transporting machinery and products.

The Chief Inspector of Factories in his Report[1] for 1945 points out that training schemes for new entrants into factories do not sufficiently emphasize safety principles. The general recommendation that men should be informed of the physical and chemical hazards of their work is much more difficult to carry out in chemical factories than would at first appear. Mere statement of hazards is not enough. Workers, ever pressed for more production, become confused by a multiplicity of instructions. What is wanted is clear and simple explanation by various experts (chemists, engineers, doctors), and then a demonstration on the plant of accident-prevention techniques, followed by practical lessons on the steps to be taken by the worker to protect his own safety and that of others. The worker must co-operate. If he cannot he should leave the industry or be placed where he can do no harm.

The Works Safety Committee of the Association of British Chemical Manufacturers have recently issued a new edition of the *Safety Rules for Use in Chemical Works*,[2] first drawn up in 1938. Presented as a series of more or less dogmatic statements, it provides a summary of all those matters which ought to be considered by works managements, and there are useful references to relevant parts of the Factories Act and the Chemical Works[3] and other Regulations. Stress is laid on the appointment of safety officers in works of appropriate size. These officers should advise heads of departments who bear direct responsibility for safety. A corollary to this might be that all such persons should undergo a proper course of training and an examination before being given these great responsibilities. It is true that engineers and chemists learn much about safety precautions by experience, especially in large organizations, but in the many small factories the situation may be very different. Safety committees, rightly insisted on in these *Rules*, can contribute much, provided that the most intelligent workers serve on them.

Before manufacturing or using new or unfamiliar materials it would seem reasonable to expect employers to obtain information on their toxicity. Some of the larger chemical firms have gone to considerable lengths in this, and the recent establishment of a toxicological unit by the Medical Research Council may be expected to meet the needs of many concerns unable to carry out their own tests.

The rules which are concerned with the establishment of health services in chemical works are on the lines more or less generally recognized as desirable. The appointment of first-aid men to deal with emergencies is the only possible expedient in small factories, but a part-time medical officer should be retained to train such men and to advise on medical matters. In factories employing 250 or more persons (on any period or shift) an ambulance room should be provided and a State-registered nurse employed.

[1] *Annual Report of the Chief Medical Inspector of Factories for the Year 1945.* London: H.M.S.O.
[2] *Model Safety Rules for Use in Chemical Works.* Part I. 3rd (revised) Edition, 1947. Published by the Association of British Chemical Manufacturers, London.
[3] *The Chemical Works Regulations.* Statutory Rules and Orders, 1922, No. 731. London: H.M.S.O.

First-aid men in such factories should have their functions closely defined and be trained not to exceed them.

One of the biggest problems in the chemical industry is to obtain the co-operation of the workers in the practice of routine ablution. The importance of this is obvious on medical grounds, but just as important is the undoubted fact that dirty workers are a menace in a chemical factory. Where workers on dangerous processes are supplied with complete sets of working clothes (under- as well as over-clothes) it is in general found that reluctance to bathe is overcome. But it is very different with other workers even when comfortable facilities are provided. There is frequently reluctance to undress, fear of colds, and anxiety to get away from the works. The medical officer has an important function to perform here, and it is not an easy one.

The A.B.C.M. *Rules* advise the provision of barrier creams to protect against dirt and skin hazards. The multiplicity of such preparations on the market is sufficient indication that a really effective cream is not available. The discouragement of dirtiness and the prevention of dermatitis depend largely on good working conditions and methods, good ablution practice, and a proper sense amongst management and workers that the chemical industry need not be as dirty as tradition has made it appear.

Medical men employed whole-time in large chemical factories have unique opportunities of making important contributions to safety as well as interesting themselves in more obviously medical matters. To have the required authority it is essential that they should either possess some chemical training or acquire by study a competent knowledge of the main chemical principles underlying the processes carried out in the factory. The more understanding of chemistry the doctor possesses, the more confidently will he be able to raise his voice in the councils of the industry.

SULPHONAMIDE COMBINATIONS AND SENSITIZATION

In a paper published in the *Journal* last year Dr. David Lehr, of New York, advocated the use of mixtures of different sulphonamides in place of single drugs.[1] He made the important observation that when such mixtures are given each drug retains its individual solubility in urine. It is thus possible by administering two or three drugs instead of only one greatly to reduce the risk of undue precipitation and hence obstruction in the kidney or urinary tract. Such mixtures also have a lower toxicity than an equal dose of a single compound, in spite of the fact that the better absorption of small doses of each compound produces higher total blood levels. Clinical experience of the use of these mixtures had also been satisfactory; they were therapeutically effective, rarely produced crystalluria, and were singularly free from toxic effects.

Dr. Lehr returns to this subject from another point of view in the opening pages of this issue. He is concerned here to inquire whether these mixtures, which he now refers to as "combinations," are more or less likely to cause sensitization than an equal dose of a single drug. It is clearly desirable first to determine so far as possible what are the factors governing sensitization when a single drug is given. In particular, how is sensitization affected by dose and duration of treatment? It would certainly appear a formidable task and might even seem an impossible one to obtain an answer to this question from the literature. Dr. Lehr has nevertheless succeeded in doing this, and presents his evidence and the authority for it in a single concise table. The only criteria of sensitization adopted are drug fever and rash, and the only drugs considered are sulphanilamide, sulphathiazole, and sulphadiazine. A point worth noting is the frequency of sensitization phenomena during the administration of sulphathiazole; it has even been proposed to abandon its use in the U.S.A. on this account.

The main conclusion, which is amply supported in connexion with all three drugs apart from one anomalous finding in the lower dosage range of sulphanilamide, is that the smaller the daily dose the less likely is sensitization to occur. This is true regardless of the duration of treatment. A small dose continued for months is unlikely to sensitize—witness the results in the prodigious number of 664,840 patients given 1 g. of sulphadiazine daily for up to 90 days. These were mostly members of the U.S. armed Forces who took part in the mass prophylaxis of respiratory tract infections attempted during the war. On the other hand, doses of 6 g. or more daily of any of these three drugs given for only a few days are much more likely to cause sensitization. The difference is slightest in the case of sulphadiazine, much the least apt of the three to produce such effects at all. It appears, therefore, that up to 2 g. daily of any sulphonamide can be given for long periods or repeatedly with little risk of sensitization; the danger is from heavy doses, usually given for only short periods in the treatment of severe infections. This is a conclusion of fundamental importance and calls for general recognition. Evidently high blood and tissue concentration favour the development of sensitization; Lehr suggests 5 mg. per 100 ml. as the level which must not be exceeded. He points out that the notorious frequency of sensitization following local application is explicable on the same lines: if the drug is applied to eczematous skin or to any wound, absorption will lead to very high concentrations in the underlying tissues. It is generally believed that sulphonamides can function only as haptenes, the actual sensitizing agent being a compound of the drug and a body protein. This view is supported by the behaviour of sulphathiazole, which has both a high protein-binding power and a marked tendency to cause sensitization. It would be interesting if it could be shown *in vitro* that combination with protein is affected by sulphonamide concentration in the manner which these clinical findings would lead one to expect.

The final step in the author's argument rests on the fact that sensitization is usually specific for a particular drug. Whether one sulphonamide or two or three are administered at the same time, the possibility of sensitization will depend on the concentration of each drug attained in the blood and tissues and not on the total sulphonamide

[1] *British Medical Journal*, 1947, **2**, 934.

concentration when more than one is given. It is therefore to be expected that sulphonamide combinations will be less likely to sensitize than the same dose of a single drug. Lehr's personal experience bears this out. He gives particulars of 610 patients treated with combinations of two or three drugs, including sulphathiazole, in whom the frequency of sensitization nowhere exceeded 2%. Perhaps more extensive experience of the method is called for before this conclusion can be finally accepted, but an excellent case has been made out for an additional advantage of sulphonamide combinations. The same principle might be applied when several compounds of related but different molecular structure have the same pharmacological action. Thiouracil derivatives are said to behave independently in the production of sensitization and might therefore with advantage be used in combination for the same reason. If the possibilities of this principle are borne in mind, other useful applications of it may well be found.

REMOVAL OF CHILDREN'S TONSILS

It is questionable whether any clinical problem has caused more controversy in medical and surgical circles or more confusion in the minds of lay people than that which was tersely stated by Kaiser in the title of his book, *Children's Tonsils; In or Out?* In a recent letter to this *Journal* Mr. T. B. Layton[1] urged that the medical profession as a whole should reconsider its approach to tonsillectomy. The operation—perhaps more correctly described in bygone days as tonsillotomy—is an ancient therapeutic measure, for Celsus referred to it about A.D. 50, and Paulus of Aegina performed it with a hooked instrument about A.D. 670. But it is only during the past thirty years or so that the operation has been performed frequently—too frequently in the opinion of many clinicians. Dr. J. Alison Glover,[2] who has recently reviewed the subject from the paediatrician's point of view, shares this opinion, and he suggests that further critical and controlled investigation of the indications for and after-results of the operation are needed.

An intelligent layman might well be surprised that doctors have not reached definite conclusions about the value of an operation which has been performed upon more than one and a half million children attending public elementary schools in England and Wales during the past twenty years; and he might argue that there should be a close season for tonsils until more is known of their functions. Though there is little precise knowledge on this point, few will deny that the location and cellular structure of the tonsils suggest that they contribute to the individual's defence against bacterial attack. They may be compared to filters, with the cervical lymphatic glands as a second line of defence. If it were possible to say from the patient's history and from direct observation that tonsils are diseased beyond natural repair there would be a good case for their removal and, if it were surgically possible, their replacement by healthy tonsillar tissue. The chief difficulty confronting the clinician is one of diagnosis. Simple hypertrophy—probably a beneficial reaction—should no longer be regarded as an indication for operation; and the history of frequent recurrences of tonsillitis is now thought to be a more valuable guide than clinical examination of the tonsils. Statistical evidence, though difficult to assess, would appear to favour a conservative attitude towards operation.

There are, however, certain aspects of tonsillectomy which justify definite statements. It is a major operation, never urgent, and it should be preceded by a period of observation of six months after the completion of any necessary treatment of teeth and sinuses; it should not be performed in winter or early spring, nor when infectious diseases are prevalent; and it seldom improves the condition of patients with established systemic diseases such as nephritis or rheumatism.

[1] *British Medical Journal*, 1948, **2**, 310.
[2] *Arch. Dis. Childh.*, 1948, **23**, 1.

RAT-BITE FEVER

There are two forms of rat-bite fever caused respectively by *Spirillum minus* and by *Streptobacillus moniliformis*, which some workers prefer to call *Actinomyces muris*. The disease has been reported from various parts of the world, but the spirillar type, which is the commoner, is specially prevalent in the Far East, including Japan, where it is known as "sodoku." There are clinical differences between the types, but the diagnosis can only be made bacteriologically. The usual history is that some days after being bitten by a rat or, more rarely, some other animal the victim succumbs to a severe febrile illness characterized by marked prostration, muscular pains, glandular enlargement, and a maculopapular or morbilliform rash. After an initial febrile period lasting two to four days the temperature subsides until the occurrence of the next bout of fever a few days later; fever of this relapsing type may last for weeks or months. The case fatality in the past has probably been from 2 to 10%.

Brown and Nunemaker[1] reviewed both types of rat-bite fever and observed that while they may be clinically indistinguishable there are certain features characteristic of the streptobacillary type. The incubation period, often only two or three days, is shorter than the usual one-to-three weeks of the spirillar disease; the fever is less regular in its relapses; joint pains and actual arthritis are common; and there are few local inflammatory signs in contrast to the spirillar type, in which the wound becomes inflamed, the regional glands enlarged, and the dark purple rash may appear around the bite before becoming generalized.

The laboratory diagnosis of rat-bite fever is made by isolation of the infecting organism from the blood or from serum at the site of the local lesion. *Spirillum minus* may be found in dark-ground preparations of blood or peritoneal fluid from mice or guinea-pigs inoculated with infected material. *Streptobacillus moniliformis* is pathogenic to mice, but can be more quickly demonstrated by culture of the patient's blood in digest or serum broth, subcultured on Loeffler's medium. The organism grows rapidly in fluid media in the form of fluffy "cotton-ball" colonies. Microscopically it consists of chains of coccobacilli and pleomorphic filaments showing beading and swellings. It is Gram-negative in young cultures. The agglutination test has been found useful in diagnosis by some workers if a uniform suspension of the organisms is carefully prepared. A leucocytosis is found in both types of disease, and a considerable proportion of false-positive Wassermann reactions have been reported, especially in cases due to *Spirillum minus*.

A report of a case of infection with *Streptobacillus moniliformis* by Dr. I. R. W. Lominski, Dr. A. Stewart Henderson, and Professor J. W. McNee in last week's *Journal* (p. 510) serves as a reminder that rat-bite fever may be a hazard of the laboratory worker. This case, which was of considerable severity, responded dramatically to treatment with penicillin. A dosage of 12,000,000 units was given over a period of seven days, but there is evidence that a smaller dosage would probably have been effective. The disease due to *Spirillum minus* responds both to arsphenamine and to penicillin. The frequent occurrence of

[1] *Bull. Johns Hopk. Hosp.*, 1942, **70**, 201.

Streptobacillus moniliformis in the nasopharynx of rats was confirmed by these authors, who found the organism in 7 out of 10 of the rats from the batch containing the original culprit. Rat bites, however, are not necessarily the only cause of human infections: two outbreaks in the United States of the disease known as Haverhill fever have been traced to the consumption of raw milk presumably contaminated with this organism.

TRAINING OF NEUROSURGEONS

The long training that a neurosurgeon must undergo before he is a competent, let alone an experienced, practitioner, and the large number of cases that now come into his hands, compel him to devote his time exclusively to their study and treatment. The Society of British Neurological Surgeons, whose planning committee under the presidency of Sir Hugh Cairns has recently issued a report on the provision and training of neurosurgeons,[1] is therefore to be congratulated on emphasizing that recruits to this important specialty should have obtained the F.R.C.S. and spent another year in the practice of general surgery. As the committee points out, "The neurosurgeon must be on familiar ground when he operates on the neck, the back, and in the retroperitoneal and extrapleural spaces." He would also gain valuable experience from spending six months as a house-officer in a department of medical or surgical neurology. Training the apprentice in neurosurgery is the next stage, and the committee considers that 4½ years are required—perhaps less for a man experienced in some other branch of surgery.

The first year of this period should be spent as a senior house-officer in neurosurgery, and the second in gaining experience of the physiology of the nervous system, or its anatomy, pathology, or bacteriology. Six months' training in medical neurology follows, and in the third year the apprentice acts as registrar in the department of neurosurgery. In the fourth year the registrar works also as a "domiciliary consultant." The last is a particularly interesting recommendation, for it would keep the registrar in close touch with the clinical problems of his specialty and at the same time help to relieve the shortage of neurosurgeons available for home visits. The committee forestalls criticism that a relatively junior man would be doing this work by pointing out that most consultations in neurosurgery are requested to decide whether the patient needs treatment in hospital or not. A training such as this, leading to a career of arduous and sometimes excessive work, is not a rosy path, as the committee frankly admits; it is perhaps strewn with rarer flowers, though, and may in future be less hazardous financially than has been the case hitherto.

Over the last 20 years the work of the neurosurgeons has increased steadily, and the committee suggests that a centre of about 50 beds is necessary to serve the needs of a million people. Regional and area centres should be created in association with the universities and the teaching or large general hospitals, not in isolation; the regional centre would have two complete surgical teams and about 50 beds, the area centre about 25 beds. The neurosurgical team would have at its head a director holding the university post of reader or professor, an assistant director also on the university staff, associate neurosurgeons, a chief assistant (registrar), and house-surgeons. There would also be anaesthetists, a neuropathologist, and special facilities for radiography and electroencephalography. Auxiliaries trained in massage and occupational and speech therapy would be required, a nursing staff rather larger than that in other branches of surgery, social workers, and a secretariat. Medical neurologists and psychiatrists must be readily available for consultation. A scheme of this magnitude might have seemed a luxury before the recent war, but there can be no doubt of its necessity now, when there are many thousands of cases of head injury alone every year—a high proportion of them sustained in road accidents.

[1] "Notes on the Neurosurgical Needs of the Population and the Training of the Neurosurgeon."

BIOCHEMICAL CHANGES IN HYPERTENSION

The search for humoral factors in hypertension continues unabated. The possibility that the suprarenal cortex may be involved has been considered from time to time because of the occurrence of high blood pressure in Cushing's disease. In a recent report Fisher and Hewer[1] draw attention to an unduly high frequency of suprarenal cortical hyperplasia in patients with high blood pressure. Perhaps allied to this is the temporarily beneficial effect of a low salt diet in reducing the blood pressure. Selye[2] has shown that experimental animals treated with desoxycorticosterone develop hypertension associated with an increase in the ratio of sodium to chloride in the serum. This was caused mainly by a decreased chloride value, though there was an occasional increase in sodium. In a series of 38 hypertensive patients it was found that the Na/Cl ratio in the serum was increased above the normal upper limit of 1.4 up to figures as high as 1.6 and over. In addition to this, the glyco-corticoids formed by the suprarenal cortex were present in the urine in increased quantities, though the 17-ketosteroids were low. The administration of ammonium chloride in doses of 6 g. daily was sometimes effective in changing the serum sodium chloride ratio towards the normal. No favourable responses, however, were obtained in hypertensive patients over the age of 50 with diastolic pressures less than 100 mm. This group probably contains those patients with arteriosclerosis affecting mainly the large vessels. Selye includes in his paper a chart showing the progress of a patient with malignant hypertension whose blood pressure fell to normal while he was being treated with ammonium chloride. This report is interesting, but there is rather too much speculation about the connexion between hypertension and rheumatism. None the less, the biochemical facts, if substantiated, should be further investigated. There is a hint here of a possible new method of treatment.

IMPROVEMENTS IN ARTIFICIAL LIMBS

Research work on artificial limbs must be very satisfying, and at the same time embarrassing; satisfactory because if one idea fails it is possible to try again with the same patient, and embarrassing because the amputees themselves are so full of ideas. According to the Second Report[3] of the Standing Advisory Committee set up by the Ministry of Pensions, no fewer than 153 suggestions were received during the year; 82 of them were worth serious consideration, the rest being discarded as impracticable or referred elsewhere because they were outside the scope of the research department's activities. Yet every proposal, even though not immediately or remotely acceptable, is acknowledged and recorded, so that nothing is lost and full credit may be given to the inventor of a useful device. Particular attention has been paid to development of the suction-socket leg, which enables a patient with an above-knee amputation to dispense with suspensory apparatus. Experiments carried out in Great Britain eighteen years ago were unsuccessful, but the Germans have had better fortune and the committee was favourably impressed with the appliances in use in Germany. There are two problems, the socket and the valve. The fit of the socket must be accurate, and, since

[1] *J. Path. Bact.*, 1947, **59**, 605.
[2] *Canad. med. Ass. J.*, 1947, **57**, 325.
[3] Published by H.M.S.O. Price 4d.

the stump is liable to changes in shape, adjustment must be easily possible. In this respect the wooden socket is the best so far, and thirty are now on trial. The disadvantage of the one-way outlet valve is that a gradually increasing negative pressure develops in the socket which ultimately damages the stump. The research department has now devised a double-acting valve and has determined what are the most satisfactory positive and negative pressures. Valves can be tested and set to give the proper pressure variations, and it is now possible to replace a valve without requiring the patient to attend the limb-fitting centre.

Great ingenuity has been displayed for many years past in the design of mechanical hands, but hitherto the controlling mechanism has been too complicated and the hand itself too heavy. However, one inventor who was given the full facilities of the research workshop, though himself failing to produce a satisfactory appliance, left his designs with one of the Ministry's contractors, who has now succeeded in producing what may prove to be a useful hand. A working liaison with research departments in the United States has led to the development of another type of mechanical hand in which only the three lateral digits are mechanically controlled; this appliance is under trial. Much care has been taken with the design of ancillary appliances such as crutches, sockets for holding tools, the tools themselves—pliers, combs, etc., telephone fixtures, and rubber sleeves for double below-elbow amputees. These sleeves enable a double amputee to bath and wash entirely unaided, and in common with many other products of the research department were most favourably received when Dr. Craft, the officer-in-charge, demonstrated them in the course of his visit to the United States and Canada last year. Preoccupation with the design of artificial limbs and appliances has left little time for the investigation of new materials in the construction of limbs, but in certain situations nylon webbing and cord have proved much superior to leather.

This second report, written with clarity and modesty, shows that this country is determined to maintain its pre-eminent position in the provision of appliances for those who have had the misfortune to suffer amputation. It is easy to say that more work could have been done had the establishment of the research department been larger; but perhaps it is best that its growth should be gradual—it is not yet three years old—and the strong advisory committee responsible for these investigations will no doubt press for expansion if and when they think it desirable.

GLANDULAR FEVER AND THE NERVOUS SYSTEM

For many years it has been appreciated that glandular fever may be complicated by signs indicating infection of the nervous system. Perhaps suspicion is most frequently aroused by severe headache. In these cases it is usual, as Lumsden's[1] experience has shown, for the cerebro-spinal fluid to be unaltered, but very rarely a neutrophil meningeal reaction may occur.[2] Less uncommon than this is a lymphocytic pleocytosis accompanied by meningitic, meningo-encephalitic, or encephalitic symptoms. Tidy[3] has found five examples recorded, and he has made the suggestion that "benign lymphocytic meningitis" is, in fact, frequently due to glandular fever. A varied assortment of cranial and peripheral nerve palsies have been noted as complicating this disease, but these nervous sequelae cannot be fitted into any clinical classification. A recent report has added yet another complication. Ricker[4] and his colleagues have described two examples of the association of glandular fever with what they term the Guillain-Barré syndrome. In both patients glandular fever was complicated by a rapidly ascending flaccid paralysis, with little or no sensory loss and without sphincter disturbance. Within a week of onset respiratory paralysis caused the death of both. Neither showed the albumino-cytologic dissociation Guillain[5] has claimed as characteristic of his syndrome, and perhaps it is wiser not to apply the eponymic label. Nevertheless here is another and a serious neurological complication to be added to the heterogeneous collection already noted during the course of glandular fever.

[1] *British Medical Journal*, 1943, **1**, 567.
[2] Shafar, J., and Weir, J. C. R., ibid., 1943, **1**, 218.
[3] *Lancet*, 1946, **2**, 819.
[4] *Blood*, 1947, **2**, 217.
[5] *Arch. Neurol. Psychiat., Chicago*, 1936, **38**, 975.

ROCKEFELLER BENEFACTIONS

In his report[1] on the work of the Rockefeller Foundation in 1947 Dr. Raymond Fosdick, the president, says that representatives of the Foundation in that year visited practically every country in the world with the exception of Bulgaria and the Soviet Union. Visas for these two countries could not be obtained, nor was it possible to establish contact with their scholars and scientists. Since the end of the war the Foundation has budgeted for the expenditure of $5,500,000 on various activities in the war-crippled countries of Europe. The aim has been first to get research started again by providing equipment or support to a few universities, libraries, and research centres, and secondly, through conferences and improved circulation of specialist journals, to re-establish the contacts of those institutions with each other and with the rest of the world.

The Foundation works in five divisions—namely, natural sciences, medical sciences, humanities, social sciences, and public health—and all have taken part in the post-war effort. The largest grants were made to Britain, France, Denmark, Holland, Norway, Sweden, and Switzerland. The recipients of grants in Britain included the Burden Neurological Institute, Bristol; Edinburgh University, for research in neurosurgery, neurology, and psychiatry; the Medical Research Council, for the purchase of scientific equipment; Cambridge University, for research in cell physiology at the Molteno Institute; King's College, London, and Leeds University, for research in molecular biology; Oxford University, for research in organic chemistry in the Dyson Perrins Laboratory and on antibiotics in the Sir William Dunn School, and for studies in agricultural economics; the Royal Institute of International Affairs, towards the expense of producing a history of the war and of the peace settlement; and the British Museum, for the establishment of a micro-film library. The Foundation had to decline 2,500 applications for financial aid during 1947. These included 18 public health projects and 70 "cures, remedies, investigations of theories, and inventions."

The largest grant the Rockefeller Foundation made in 1947 was $10,000,000 to the China Medical Board. This is one of the Foundation's oldest interests. The China Medical Board, which was created in 1914 as an operating division of the Foundation, was responsible for the erection and development of the Peking Union Medical College, one of the world's important medical training centres. The college has lately been reopened, after its deterioration in the hands of the Japanese, though it is working under far from perfect conditions. The China Medical Board is empowered to give financial support to other similar institutions in the Far East or even in the United States, but so long as opportunity remains for effective work in the College in Peking that is its first responsibility.

[1] *The Rockefeller Foundation—A Review for* 1947. 49, West 49th Street, New York.

MEDICINE AS A PLANNED ECONOMY

THE BIOCHEMIST'S VIEW

BY

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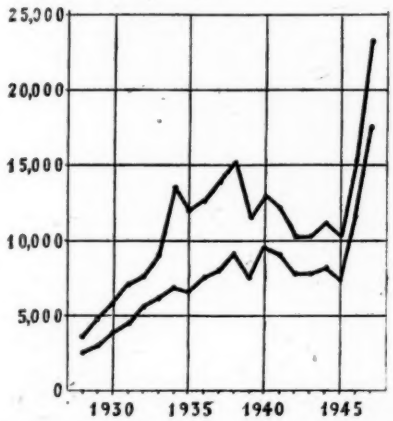
In a recent paper entitled "Where Are We Going?" Roberts (1948) has commented on the extraordinary increase in the number of patients submitted to *x*-ray examination, and he very aptly describes the work of an *x*-ray department as "accelerating towards infinity." The biochemistry department suffers in the same way, and in this laboratory we have encountered a similar extraordinary increase in the number of specimens submitted for analysis. The graphs shown here are exactly comparable to those in Roberts's paper. The total number of



Total number of analyses (upper graph) and total number of blood analyses (lower graph) during the period 1928–47.

analyses carried out annually reached a steady level about the year 1933, and maintained this level, averaging about 12,000 per annum, without much fluctuation until 1945. In 1945 the total number of analyses was 10,384; in 1946 it rose to 15,203; and in 1947 it rose again to 23,218.

During the last two years the process of "acceleration towards infinity" has forged ahead to such an extent that one is forced to draw the only logical conclusion—that, unless this acceleration stops, the doctors of the near future will be concerned solely with the problem of collecting specimens to the exclusion of all other forms of practical medicine. This is a far more serious threat to the art and practice of physic than any Government legislation, and to the non-clinical onlooker it is a tragedy that the teachers of to-day do so little to arrest this degeneration of modern medicine. The taking of a good history and the recording of the results of a careful clinical examination should be the main duty of every junior clinician: the collection of a large bundle of assorted laboratory reports ought to be regarded as an indication that the doctor's clinical knowledge and powers of observation are deficient in certain respects. Some laboratory examinations are so valuable that they now form an essential part of medical practice, but they are comparatively few in number. It is the duty of every clinician to find out what these methods are, to use them properly, and to avoid the others.

There are many factors at work in this recent development of hospital biochemistry, and it is interesting to classify the main sources of the trouble.

Factors in the Biochemist's Burden

First, there is the natural desire for the clinician to produce as complete a case history and examination as possible. This leads to the sending of specimens to the pathology, bacteriology, biochemistry, and haematology departments with sundry requests, while the patient is sent to the *x*-ray department with instructions to have an electrocardiogram done on the way back to the ward. This type of investigation often has its origin in the self-recrimination undergone by the doctor who has, at a less experienced stage in his career, failed to detect a lesion which might have been spotted had he carried out some simple laboratory examination. He is, quite rightly, determined not to make the same mistake twice. But he should remember that no case history can ever be complete.

Secondly, there is the type of doctor who must have as much laboratory confirmation as possible for every clinical diagnosis, irrespective of any signs or symptoms. If a patient is in the terminal phase of chronic nephritis there is little point in taking a specimen of blood for determination of urea, creatinine, cholesterol, and alkaline phosphatase. Even the teaching value of such analyses is small.

Thirdly, there is the clinician with an inquiring turn of mind who would be better described simply as a "figure-collector"—a snapper-up of unconsidered analyses. All biochemists are painfully familiar with the type who approaches him at frequent intervals with a request to churn out a series of analyses of, say, the blood lactic acid in a thousand consecutive cases of prolapsed polycystic kidney. The number of such workers unacquainted with the *Index Medicus* is remarkable. A variant of this species is the investigator who refuses to accept the standards quoted in the literature. He is determined, at any cost, to have a series of analyses of his own, although quite prepared to use the established methods on a series of cases exactly similar to those studied by other workers.

Fourthly, there is the group who wish to practise venepuncture. They are to be commended, not condemned, for they are endeavouring to master a technique. But is it necessary to send the sample to the biochemist with a request that he determine the "B.U.N." (*anglicè*, blood urea nitrogen)?

Fifthly, there is the type of clinician who annoys the laboratory with analyses under the impression that the results are of diagnostic or prognostic importance, when in actual fact the results are of neither scientific value nor clinical significance. The biochemist certainly bears the brunt of this type of work. A barium meal on an elderly gentleman with some gastric disturbance may be negative, but the negative result is of great value to both doctor and patient. A blood-urea estimation is of absolutely no value whatever in 95% of the cases in which it is done.

Lastly, there is a comparatively small group who can give no reason whatever for having sent a request for certain analyses, and when the matter is discussed with them they are quite agreeable to the specimens being discarded.

There are many other subsidiary causes of the extra burden placed on the modern laboratory. Analyses which are repeated at regular time intervals arouse no enthusiasm in the scientific mind unless the time interval corresponds to some alteration in the metabolism of the patient. And yet a clinician who repeats an analysis every twenty-four hours would be highly indignant if anyone were reckless enough to suggest that he is really trying to correlate metabolism with the movement of the solar system.

Biochemical forms which detail the amount of blood required for the commoner analyses may help to eliminate technical sources of trouble, but they are a psychological blunder, since they suggest analyses which are of no real value in the case which is being investigated. There is always the type of mentality which says, "We might as well have the potassium done at the same time." This argument is valid only in the examination of the cerebrospinal fluid, where every additional lumbar puncture carries the risk of a meningeal infection, however careful the operator.

The biochemistry department suffers from another peculiar disadvantage—it expresses its results in terms of simple figures, and in the various branches of general medicine one is frequently (or shall we say always) as far away from things mathematical as it is possible to get without entering the field of pure philosophy. The attempt to correlate the patient's changing condition with a series of changing numbers is a natural one, but it is seldom very helpful.

The final result of all these factors may be summed up in one sentence the truth of which cannot be denied: *If this "acceleration towards infinity" continues unchecked without a simultaneous and corresponding increase in laboratory facilities and staff, then the accuracy (and hence the value) of all biochemical analyses will accelerate towards zero.*

A Pernicious Trend

The pernicious effects of the modern trend to reduce clinical work to a series of reports has its repercussions in the ward and in the operating theatre as well as in the laboratory. A pathologist who recently visited Edinburgh from a distant part of the Empire produced the startling information that the surgeons with whom he is associated will not operate on any case unless the patient's blood sugar and blood urea have first been determined. In consequence he has had to employ an all-night staff so that these estimations may be made before even an emergency operation for acute appendicitis will be carried out.

In this country it is a common procedure to determine the blood urea before certain types of operation—e.g., suprapubic drainage, prostatectomy, etc. Whether or not these results are ever taken into *serious* consideration is a point on which I am not quite clear; but it is a solemn thought that some unfortunate patient may have the question of operation partly decided by a skilled technician who is fighting an increasingly hopeless battle against time and who is surrounded by a multitude of requests for analyses 90% of which can be classified only as rubbish. A colleague, recently returned from abroad, tells me that in some of the hospital laboratories which he visited the biochemistry department is divided into two sections: a small part of the work which is judged to be of importance is carefully carried out by a highly trained and experienced staff, the rest is dealt with by junior trainees. It is a pity that a scientific subject should be driven to such practices. Many would reply that the obvious procedure is to extend laboratory facilities as much as may be required to cope with the work. This is no answer. Geometrical progressions are tricky things to handle; once the indices are removed and the answer reduced to a simple number the result is astounding.

Unfulfilled Hopes

Nor can this recent fantastic increase in the number of biochemical analyses be defended on the grounds that more reliable procedures for investigating disease have been evolved in the last few years. The reverse is the case. Thirty years ago, when biochemical investigation was getting into its stride, great hopes were entertained that here we would have a truly scientific method of investigating and assessing disease reliably. These hopes have not been fulfilled, and the disappointment is not a reflection on biochemistry. Experienced biochemists realize that very little (? 5%) of the so-called "routine biochemistry" is of any value to anyone, and since the task of collecting specimens is a self-imposed one the clinician who raises a complaint against the increasing number of forms to be filled up receives little sympathy from the biochemist, who receives more than his fair share of them.

The argument that the clinician sees the patient while the laboratory staff do not is an argument which often carries far too much weight. Consider the following typical case:

Patient: Male, aged 36.	Specimen: oxalated venous blood.
Diagnosis: Myocarditis.	Investigation required: plasma proteins.

The biochemist accepts the diagnosis as correct. So far as he is concerned, it is quite sufficient that the patient's symptoms even suggest the diagnosis which is given. If the patient has an infective condition such as myocarditis it can safely be assumed that the plasma albumin will be a little below normal, the globulins will be normal or slightly raised, and the fibrinogen will be normal. We may therefore ask three questions: Irrespective of the actual figures obtained on analysis (i.e., the extent of the deviations, if any, from the normal), will the report (*a*) modify or cancel the physician's diagnosis? (*b*) affect in any way the physician's prognosis? (*c*) affect the treatment of the patient in any important detail? The answer in each case is an emphatic "No!" Such examples could be multiplied several thousand times over per annum.

A wholesale condemnation of modern biochemical analyses may lead the clinician to conclude that laboratory staffs regard their departments as superfluous hospital appendages. There is a germ of truth in the conclusion. Most departments dread the day when hospital laboratories will be open to the outside consultant and to the family doctor. If these two classes of doctor send in an amount of work proportional to their numbers (and there is no valid reason why they should not), then every laboratory in the country will be reduced to complete chaos.

The Question of Blood-urea Analysis

Much of the congestion in the biochemistry department is caused by a multiplicity of requests for determinations of the blood urea. During the past 20 years blood-urea estimations have formed about one-third (22–39%) of the total number of biochemical analyses in this laboratory. Of the first thousand reports sent out at the beginning of this year no fewer than 533 contained blood-urea analyses. An examination of the diagnoses sent on the accompanying forms is of some interest:

	Total		Percentage
No diagnosis given	62		12
Prostatic hypertrophy	29	95	18
Other diseases of the renal tract	66		
Hypertension	74	137	26
Other cardiovascular diseases	63		
Other diagnoses not included above	239		45

In only two of these 533 analyses was the blood urea part of a van Slyke urea-clearance test. The 239 unclassified diagnoses were described under 64 different diseases or symptoms. The commonest were: pre-eclamptic toxaemia (21 analyses), diabetes (20), thyrotoxicosis (15), haematemesis (13), peptic ulcer (11), jaundice (8), hepatic cirrhosis (7), bronchitis (7). Other diagnoses included iritis, sciatica, asthma, hysteria, dyspepsia, sarcoidosis, silicosis, epilepsy, leukaemia, polycythaemia vera, anaemia, spondylitis ankylopoietica, exfoliative dermatitis, scurvy, trigeminal neuralgia, and abdominal pain.

A random blood-urea analysis is probably the most useless and, at times, the most misleading of all laboratory examinations. Its great popularity appears to rest on the following points: (1) No other constituent of blood is so definitely associated in the mind with an anatomical system as the urea is with the renal tract. (2) The renal system cannot be examined adequately at the bedside. (3) A complete examination of the renal system *must* include certain laboratory tests—e.g., examination of the urine. (4) There is a popular impression that the blood urea is a measure of the patient's renal function. This belief was abandoned about 30 years ago by biochemists. (5) The blood urea is elevated in so many diverse pathological conditions that it is the laboratory test *par excellence* which is most likely to give an abnormal result when done at random. Of the 533 blood-urea-nitrogen analyses referred to above, 62% were over the normal upper limit of 15 mg. per 100 ml.

There is little space left to consider two other important aspects of this problem. First, a laboratory inundated with routine analyses has no time to spend on the more elaborate methods used for research: the quickest methods are the best. Secondly, there is the question of expense.

Conclusions

Everyone must agree that the alarming increase in the number of laboratory examinations must stop or be stopped before things reach the stage of becoming a farce. It would give rise to a good deal of acrimonious debate whether the process should be stopped by the clinician, by the laboratory staff, or by the hospital authorities, and whether it should be stopped by innuendo, persuasion, coercion, or compulsion. I do not propose to allow myself to become entangled in this delicate point.

It is a great pity that there is not more collaboration between clinical and laboratory staffs. Active co-operation could do much to root out obsolete and unnecessary work, and in other cases investigations which are of importance could be substituted with advantage to all.

REFERENCE

Roberts, F. (1948). *British Medical Journal*, 1, 485.

RADIOACTIVE ISOTOPES FOR CLINICAL RESEARCH

The Medical Research Council has made arrangements to obtain from the United States Atomic Energy Commission limited quantities of certain radioactive isotopes for medical research, including therapeutic investigations. Further, it is expected that regular supplies will soon become available from Canadian sources and later from British sources.

The Medical Research Council now invites institutions to submit for consideration detailed programmes of research in the clinical field. The application should include adequate information on the following matters :

(*a*) Specification of the radioactive isotope required.
(*b*) Quantity desired. (Radioactive isotopes with half-lives of less than 30 days may be allocated in fulfilment of one request, in amounts sufficient for six months' needs, with arrangements for shipments at intervals of not less than one week.)
(*c*) Date and rate of deliveries desired.
(*d*) Name of institution at which the materials will be used.
(*e*) Names and research experience of investigators who will use the materials. This list should include the names of the radiotherapist and physicist who will collaborate in the research.
(*f*) Purposes for which the materials will be used, with methods of administration and the dosage required.
(*g*) Protection and safety measures to be employed to safeguard the health of the workers. (Useful guidance will be found in *Introductory Manual on the Control of Health Hazards from Radioactive Materials*, which may be obtained from the Medical Research Council on application.)
(*h*) Proposed financial arrangements, including the sources from which the applicant will defray the cost of the materials.

Information under these headings, except (*h*), is required by the United States Atomic Energy Commission as a condition for the supply of the isotopes. The Commission supplies isotopes only for accepted lines of research of which the results are fully published and which are conducted in institutions open to visits from investigators in this field of all nationalities. The Medical Research Council should for this reason be notified of any such visits by workers from other countries to any institution receiving the isotopes through its agency.

Progress reports must be made to the Medical Research Council every six months. In the case of therapeutic investigations the institution supplied with radioactive isotopes must undertake to register the patients treated according to the cards and system of the Statistical Department of the General Register Office.

In its application to the Medical Research Council for radioactive isotopes the institution must give the following undertakings :

1. That the materials supplied will not be used in any manner other than that disclosed in the application.
2. That the institution will maintain all necessary protection and safety measures to avoid the special hazards to health arising out of possession, handling, and use of radioactive isotopes, and will allow inspection of all such protection and safety measures by representatives of the Medical Research Council.

The Medical Research Council wishes to emphasize that the supplies of radioactive isotopes are at present limited and that the materials are costly, especially on account of charges for transport.

It is expected that the isotopes in greatest demand will be radio-phosphorus, P^{32}, and the radio-iodine, I^{131}. The following information about the preparations of these two isotopes available is given by the United States Atomic Energy Commission.

Phosphorus^{32}.—Half-life: 14.3 days. Beta radiation 1.71 mev. Supplied as phosphate ion probably in the form of Na_2HPO_4 in a solution containing 0.5 to 3 millicuries per millilitre. Chemical analysis is furnished with each shipment. Material will meet the following specifications:

Concentration	Greater than 0.5 mc./ml.
*p*H	7–9
Total solids	Less than 10 mg./ml.
Non-volatile matter	Less than 5 mg./ml.
P (inert)	Approximately 0.025 mg./mc. added. (Carrier-free material is available if desired).
Cl	Less than 5 mg./ml.
Fe, Ni, Al	Content so low that no precipitate is formed at *p*H 7–9

Iodine^{131}.—Half-life: 8 days. Beta radiation 0.6 mev. Gamma radiation 0.367, 0.080 mev., and probably also 0.65 mev. (10–15%). Carrier-free, in neutral or weakly basic solution containing 0.3 to 2 millicuries per millilitre. Chemical analysis is furnished with each shipment. Material will meet the following specifications:

Concentration	Greater than 0.3 mc./ml.
*p*H	7–9
Total solids	Less than 1 mg./ml.
Te inactive	0.1 mg./ml.
Te active	Less than 1×10^{-4} mc./ml.

The Medical Research Council will not accept responsibility for the accuracy of the statement as to radioactive content which will accompany each sample or for the freedom of the sample from toxicity.

The cost of the materials will depend on various factors, including the extent of the demand, but is unlikely in the first instance to be less than £1 per millicurie for I^{131} or 10s. per millicurie for P^{32}.

While every effort must be made to utilize these therapeutic developments and possibilities to the full, there can be little doubt that, from the long-term point of view, the treatment of cancer and allied diseases is most likely to be advanced by the encouragement of tracer investigations, using both radioactive and non-radioactive isotopes. Materials for this purpose are also obtainable from the Medical Research Council, and at present, in view of the small quantities involved, no charge is being made.

The need for extreme caution in the clinical use of radioactive isotopic tracers cannot be overemphasized. The safety of non-radioactive tracers should recommend their use in clinical investigations.

Dangers and Limitations of Radioactive Isotope Therapy

Certain dangers inherent in radioactive isotope therapy are becoming recognized, especially in the case of radio-phosphorus administered internally as inorganic phosphate. The most serious of these are possible injury to the reproductive organs, genetic damage, the induction of leukaemias and the hastening of the appearance of leukaemic conditions, and the production of malignant tumours. The leukaemogenesis and carcinogenesis, including induction of sarcoma of bone, are likely to be delayed effects, with a long latent period of possibly five years and probably often longer. Accordingly, in the present state of knowledge it is usually unwise to employ radio-phosphorus in the treatment of patients of either sex in the reproductive period of life or in patients whose expectation of life exceeds five years.

In general, it must be concluded that therapeutic trials of radioactive isotopes should be limited to cancer and allied diseases and to polycythaemia vera. With rare exceptions radioactive isotope therapy should not be used in non-malignant conditions. Further, the opinion has been expressed that, in the present state of knowledge, radioactive isotopes should in no case be used in the treatment of children suffering from non-malignant diseases.

Despite these limitations, there is an important field of investigation of the therapeutic applications of radioactive isotopes. At first it will be necessary to develop techniques and to confirm and extend the results of the American workers, while profiting from their experience. Subsequently it seems likely that the development of selectively concentrated organic compounds containing radioactive isotopes may be a promising line of investigation. Probably there will be an immediate though rather limited field for the use of external applicators containing sources of beta rays. Experience of the use of artificial gamma-ray sources, such as radio-cobalt ($cobalt^{60}$) in radiotherapy is at present very restricted, but this is a matter for experimental development when adequate regular supplies become available.

All correspondence should be addressed to the Secretary, Advisory Panel on the Allocation of Radioactive Isotopes for Clinical Research, Medical Research Council, 38, Old Queen Street, London, S.W.1.

Tridione has been added to Part 1 of the Poisons List and to the 1st and 4th schedules to the Poisons Rules. The percentage limit in respect of codeine in the 1st schedule to the Poisons Rules has been raised from 1 to 1.5.

INDUSTRIAL MEDICINE

NINTH INTERNATIONAL CONGRESS OPENED

The Ninth International Congress on Industrial Medicine, which met from Sept. 13 to 17, is the first to be held in Britain. Their Majesties the King and Queen are patrons. Congresses have been held under the auspices of the Commission Internationale Permanente pour la Médecine du Travail every four years, with intervals only during the two world wars, since the International Commission was founded in 1906 by Luigi Devoto in Milan. Lord Moran, P.R.C.P., was in the chair and introduced the two speakers who delivered the inaugural addresses—the Rt. Hon. G. A. Isaacs, M.P., Minister of Labour and National Service, and Mr. T. E. A. Stowell, President of the International Commission. Over 900 delegates from 44 countries had assembled in the Central Hall, Westminster.

Lord Moran started by saying that Their Majesties had sent a telegram expressing sincere thanks for the message of loyal greeting from the Congress and their best wishes for its success. Some of the delegates had come to learn what the others could teach them from their own particular experience and some to study the organization of an industrial medical service. We now had a health service available to all; we hoped presently to have a universal industrial health service for all who needed it. That service would come under the Ministry of Health.

They were all interested in the education of doctors who were going to take part in industrial medicine. Some thought the medical education of the undergraduate should include training for industrial work, but he could not agree. Medical education should be general and specialization should come later. He was surprised that so little attention was paid to the teaching of normal psychology in medical schools, but he disagreed with people who said that medical practice of that kind was inefficient only because of inadequate training. Often it was not lack of training so much as lack of imagination that prevented men from taking an interest in the psychology of the worker. It was necessary to study the minds of workers, and he gave as an instance the present shortage of nurses. Recent reports had shown that the nursing profession was receiving an inadequate number of recruits partly because of the working conditions, yet who was responsible for advising about those conditions but the medical staff? He then pleaded for more fundamental research to be done, and pointed out that the research worker who did not concentrate on finding the solution to a particular problem was nevertheless generally the man who solved our everyday problems. However, the Industrial Health Research Board had produced some 80 papers on industrial fatigue and hours of work, yet when the second world war came their conclusions had been completely ignored.

Turning to the question of incentives in industry, a problem much discussed at present, he thought that perhaps the best incentives lay not in wages but in human relationships, which he likened to the spirit that pervades a battalion in wartime. The industrial medical officer had a unique opportunity for studying group morale. Why had some men failed to adapt themselves to their surroundings? Medical officers must investigate and assess such factors as loss of interest and boredom. They must find the explanation for loss of harmony, for if men were contented you got increased production.

Mr. G. A. Isaacs said that on looking through the programme of the Congress two things in particular had impressed him—the wide range of the diseases to be discussed and the fact that papers were not limited to strictly medical problems. Discussion was not intended to be narrow or academic. Medical officers working in special climatic environments—whether hot or cold or, as in Britain, sometimes hot and sometimes cold and always wet—would have the opportunity of exchanging views. Though appreciating the practical approach to the problems of industrial medicine shown by the Congress, he did not minimize the importance of the academic side. He knew how desperate the need was for more trained men and women. Industrial medicine had long received a good deal of attention in Britain. We had been first in the field in the development of industry and the first in dealing with the diseases that arose from it.

He strongly supported the formation of a national industrial medical service, and said that it was part of the Government's policy. It depended on how soon they could get enough doctors. The mere appointing of doctors to factories did not make a service, for it depended much on specialized teamwork. At present the shortage of suitably qualified medical men was a grave obstacle. Facilities should be provided for postgraduate study, and he emphasized in particular the part that universities might play.

Mr. T. E. A. Stowell welcomed the delegates and displayed a scroll of greeting from the University of Paris; he also read a telegram from Professor E. L. Collis, who wished that the harvest the Congress would reap should be not British but international. Ours had been the first country to introduce legislation controlling conditions of work, and during the 36 years that he had practised industrial medicine he had noticed a considerable change of attitude to it on the part of employers. The Congress would allow the delegates to learn about each other's work and enable them to move towards the light of fresh understanding.

Reports of Societies

JOINT MEETING OF AMERICAN, BRITISH, AND CANADIAN ORTHOPAEDIC ASSOCIATIONS

In spite of dollar difficulties the American, Canadian, and British Orthopaedic Associations for the first time held in Quebec in June a joint meeting. By the generosity of the Nuffield Foundation and the American Orthopaedic Association and other friends 13 of the younger British orthopaedic surgeons were enabled to attend the meeting and to undertake a magnificently organized six weeks' tour of North American centres. Those fortunate enough to attend have returned with a lively appreciation of Canadian and American hospitality and a determination that something should be done towards returning it on this side of the Atlantic in the not too distant future. Dr. R. I. Harris (Toronto), President of the American Orthopaedic Association, Mr. Alan S. Malkin (Nottingham), President of the British Orthopaedic Association, and Dr. Edouard Samson (Montreal), President of the Canadian Orthopaedic Association, presided.

Joints

In a discussion on the treatment of slipping of the upper femoral epiphysis Dr. S. KLEINBERG advocated early elimination of the epiphysial plate by drilling and Dr. BECKETT HOWORTH by bone pegging. Dr. PHILIP WILSON (New York) advocated the Smith-Petersen nail for this purpose, and Dr. ALBERT KEY (St. Louis) considered that it should be placed as low and as far back as possible. Dr. CLARENCE H. HEYMAN (Cleveland) confirmed the good results of early epiphysial fusion. In late cases Drs. ARMIN KLEIN, ROBERT J. JOPLIN, JOHN A. REIDY, and JOSEPH HAMELIN (Boston) advocated osteotomy at the site of the epiphysial plate through an anterior incision.

Dr. A. B. LE MESURIER (Toronto) reviewed developmental coxa vara, which was much less common than congenital dislocation of the hip and might be satisfactorily treated by intertrochanteric osteotomy, which was usually followed by speedy closure of the gap in the femoral neck. Dr. WILLIAM T. GREEN (Boston) thought that this treatment should be accompanied by an adductor myotomy in order to ensure sufficient adduction. In adult cases Dr. ALBERT KEY had chiselled away the great trochanter without much further weakening of the adductors.

Dr. ALEXANDER GIBSON (Winnipeg) reviewed 104 cases of vitallium-cup arthroplasty of the hip carried out through a Kocher's posterior approach. The results were: good 55, satisfactory 21, poor 14, and unclassified 14. Dr. PAUL C. COLONNA (Philadelphia) doubted whether a posterior approach would allow the anterior tissues to be dealt with adequately, and Dr. M. N. SMITH-PETERSEN (Boston) expressed a similar doubt about the acetabulum. Mr. H. A. BRITTAIN (Norwich) demonstrated his method of ischio-femoral arthrodesis, saying that bony fusion was obtained in 84 out of 95 patients. He mentioned some of the complications, and other speakers emphasized the vulnerability of the sciatic nerve, especially in cases with flexion deformity.

Dr. JUAN A. FARILL described an operation for open reduction of cases of congenital dislocation of the hip otherwise irreducible. Wide exposure of the joint was followed by subtrochanteric femoral shortening and, if the acetabulum was shallow, by an extra-articular shelf. Some commentators thought the operation too drastic. Mr. F. C. DURBIN (Exeter) advocated arthrography in congenital dislocation of the hip as part of the examination in every case, because of the importance of pathological anatomy both before and after reduction.

Dr. W. E. GALLIE (Toronto) described a method of arthrodesis of the ankle-joint by the insertion of tibial grafts as mortises. Dr. DALLAS B. PHEMISTER (Chicago) and Dr. THOMAS BEATH had carried out a similar operation on the knee and Dr. ALBERT KEY (St. Louis) in the sub-talar joint. Mr. JOHN CHARNLEY (Manchester) had performed compression arthrodesis of the knee after the manner of Dr. Albert Key and had found the junction to be solid as early as the twelfth day after operation.

In a discussion on arthroplasty of the knee it was emphasized that careful selection was imperative; then the results of the operation were usually satisfactory, though functional adaptation might take five years, after which the condition usually remained stable for a long time. Until the advent of penicillin gonorrhoeal arthritis had proved the commonest indication. Ankylosis from rheumatoid or tuberculous arthritis or from old osteomyelitis was unsuitable. The limb must have good musculature and the patient a stout heart.

Mr. T. J. FAIRBANK (Oxford) had studied the changes in the knee following meniscectomy and had found radiological changes, described as a marginal ridge, flattening of the femoral condyle, and narrowing of the joint space. In the normal person the thickness of the articular cartilages diminished with weight-bearing and recovered in the intervals. Mr. I. S. SMILLIE (Edinburgh) had interpreted as discoid menisci 28 among 1,300 menisci removed. He discussed the causes of "snapping knee." Tears were much commoner, particularly ones complicating a horizontal rift, which resulted from the grinding action exerted by the condyles on the more primitive and complete type of discoid meniscus.

Dr. ROBERT I. HARRIS (Toronto) and Dr. T. HEATH (Columbia) had found that many cases of spasmodic flatfoot presented a developmental anomaly—namely, a talo-calcaneal bridge, which could be revealed by postero-superior radiography.

Trauma

Dr. EDWARD L. COMPERE (Chicago) opened a discussion on aseptic necrosis of bone after injury by referring to the slow union after fractures in which an intermediary fragment of cortical bone is deprived of its blood supply. Dr. DALLAS B. PHEMISTER (Chicago) discussed the results of aseptic necrosis of cancellous bone as exemplified by the femoral head. In such cases he had tried to accelerate revascularization by inserting tibial grafts in addition to threaded wires. Results were encouraging and were confirmed by Mr. JAMES PATRICK (Glasgow), who combined Smith-Petersen nailing with grafting

In a paper on the treatment of cervical fractures and fracture-dislocation Dr. WILLIAM A. ROGERS (Boston) advocated the use of skull traction, supplemented in most cases by wire fixation of the involved vertebrae and grafting with bone chips. Twenty of twenty-one grafts underwent fusion in a period averaging four months. In the treatment of fracture-dislocation of the pelvis, Mr. F. W. HOLDSWORTH (Sheffield) combined traction with the use of an encircling sling. The results were much better if the sacro-iliac joint had escaped dislocation.

Dr. E. HOWARD WILSON (Columbia) advocated screws and, when necessary, plates as the treatment of choice in fractures of the shaft of the femur or for fixation after limb-shortening operations. Full movement was restored within six months. Dr. E. C. JAMES (Hamilton) had found the use of external pin fixation a solution of many of the problems presented by infected war wounds with compound fractures. Mr. W. GISSANE (Birmingham) described the organization of an accident service as exemplified by the Birmingham Accident Hospital.

Neuro-orthopaedic Conditions

Professor STEN FRIBERG (Stockholm), in an anatomical investigation of lumbar disk degeneration, had confirmed the instability between vertebrae bordering a ruptured intervertebral disk. Degenerative changes were most pronounced in the anterior part of the disks except the fourth and fifth, in which they were mainly posterior. One or other of these two disks showed protrusion in 11 of 100 spines of patients of various ages examined after death.

Dr. K. G. MCKENZIE and Dr. F. P. DEWAR (Toronto) had found that in scoliosis with paraplegia the scoliosis was usually severe and congenital, though sometimes idiopathic or, less often, due to poliomyelitis, rickets, or neurofibromatosis. If there were no early response to conservative treatment the paraplegia called for surgical division of the dura mater.

Mr. F. G. ST. CLAIR STRANGE (Canterbury) showed the result of a case of ulnar and median nerve defect, too great for end-to-end suture, in which he had bridged the median nerve defect with a pedicled nerve graft from the ulnar nerve, with a success equal to the best which could be expected from end-to-end suture.

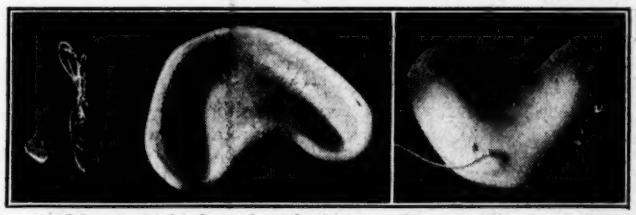
Dr. MARY S. SHERMAN (Chicago), speaking of oestrogens and bone formation in the human female, referred to the hypercalcaemia associated with ovulation and the formation of an egg-shell in certain birds. This was preceded by intramedullary hyperossification, and was not a parathyroid function, the ionized blood calcium being unaltered, but could be produced by oestrogens. Post-menopausal osteoporosis might result from deficiency of these and be relieved by their administration.

Preparations and Appliances

A MOUTH-SHIELD FOR USE WITH THE BRONCHOSCOPE OR LARYNGOSCOPE

Dr. JOHN HALLAM, of Liverpool, writes: Injury to the upper teeth or alveolus is at times an almost inevitable mishap with the use of a bronchoscope, and rather less often with a laryngoscope. The more common accidents are, in order of frequency: (1) the dislodgment of loose teeth, especially deciduous teeth which are about to be shed; (2) chipping of the enamel of one or more of the upper teeth, usually an incisor, or dislodgment of crowns and inlays or even, on occasion, sound teeth; and (3) in edentulous patients, bruising or crushing of the upper alveolar margin by the bronchoscope as it is moved around the bronchial tree. While many of the accidents in the first group can be avoided by pre-operative dental treatment, this procedure is not always possible, nor, occasionally, is it in the best interest of the patient. For example, the extraction of all slightly loose teeth in a patient who is found on bronchoscopy to have an inoperable bronchial carcinoma is only going to add to his burden.

To circumvent these mishaps a series of mouth-shields of various sizes and shapes, suitable for all classes of dentition, have been made. They are constructed from soft plastic into



Mouth-shield for edentulous case — Reverse side of mouth-shield

which is embedded stainless-steel gauze. This gauze provides the necessary rigidity without bulk, and it increases the value of the buffer action by spreading the thrust of the instrument over several teeth. In case the shield itself should become dislodged (this eventuality has not yet been met with) a plaited silk ligature is attached to it and left hanging over the table, a small lead weight having been tied to the distal end. The shields may be sterilized by boiling, and no injuries have been encountered since they were taken into use several months ago. Various shapes and sizes can be made, and dental impression trays have been found useful for the making of suitable models. It should be possible for any dental laboratory to make them.

Correspondence

Scientific Medicine in Britain To-day

SIR,—There is much to command assent in your leading article on "Scientific Medicine in Britain To-day" (Sept. 4, p. 479), but I ask your permission to make two critical comments thereon, one historical and the other on general grounds.

Historically, your survey, though of necessity brief, is presumably intended to be comprehensive. It tells the reader that "fifty years ago clinical medicine was for the most part a subject separate from or unconnected with physiology," and that clinical work of scientific quality was being pursued "almost in isolation for twenty years" by Sir Thomas Lewis. May I therefore bring to your notice the achievements of the British school of clinical neurology, a school now some eighty years old and in continuous and fruitful scientific activity since its foundation? It has made contributions of fundamental quality to the anatomy and physiology of the nervous system, to pathology, and to nosography.

I do not propose to burden your pages with the record of the labours of this school, but the present generation has seen in the field of the physiology of sensation the work of Henry Head and his collaborators, of Holmes, and of Trotter and Davies; in the analysis of cerebellar function and of the cortical representation of vision that of Holmes; and in the study of the basal ganglia that of Kinnier Wilson. In the field of nosography its clarifications, clinical and pathological, are scarcely less noteworthy.

It has to be admitted that all this has been the work of practising clinicians, amateurs if you will, carried on with neither salaries nor subsidies, nor with that growing multitude of secretarial and technical assistants that now seems to be essential to even the most modest of medical research projects. Nevertheless, a survey of the field of scientific medicine that omits mention of it can hardly be regarded as balanced or as giving a true perspective, while the quotations from your article that I have given show that it is inaccurate and historically unjust. It is not necessary thus to seek to enhance the distinction of Lewis's work, the brilliance and quantity of which stand in no need of the fictitious background of a scientific void in clinical medicine which, with more artistry than accuracy, you have created for it. Secondly, I submit that your article betrays, both historically and philosophically, an artificial conception of the relations between clinical medicine and physiology, between physicians and physiologists. They are not separable in the naïve fashion you propose.

The few instances I have given of the work of clinical neurologists constitute discernments and rational formulations of dynamic properties of the human organism elicited in the course of clinical work, and to imply that they are parts of physiology but not of medicine and that those who did this work are rather physiologists than physicians is surely no more than a misleading linguistic exercise seeking to produce distinctions where they do not exist and to make medicine appear as a derivative of physiology. I submit also that "habits of deep thought and scholarly reflection" are not to be thought of as the necessary fruits of a deliberate consecration to "research discipline." Is there no discipline of accurate observation and logical induction in medicine apart from research?

In brief, I suggest that your article places too much reliance upon planning and takes too little cognizance of the human material being planned for over its head. The theme you adumbrate is indeed of vital importance to such future as British medicine can now look forward to under its new regime of external organization, but it surely needs to be more profoundly contemplated and more clearly expounded if it is to bear fruit.—I am, etc.,

London, W.1. F. M. R. WALSHE.

Globin Insulin—A Criticism

SIR,—In your issue of July 24 (p. 191) Dr. G. M. Wauchope published a paper strongly extolling globin insulin, one daily injection, as the ideal treatment for almost all insulin cases. Professor D. M. Dunlop and Dr. J. B. Donald (Aug. 14, p. 352) from Edinburgh have criticized her optimism. I would add my fairly wide experience of globin insulin to support their opinion.

Dr. Wauchope states that globin insulin is identical in its delayed action with Dr. Hagedorn's original protamine insulin (retard, 1935). This I am sure is true and makes me ask her how it can act for 24 hours without grave risk of hypoglycaemia, which I have too often seen before the midday meal or in the afternoon, with a heavy relapse of the diabetes at night. Animal tests too show that the delay in its action is very little different from ordinary soluble insulin. The Danes and Hagedorn were factual enough to know in 1935 that their new "retard" insulin (= globin insulin) was an impossible treatment given once a day to severe diabetics, and they gave it in the evening with soluble in the morning. Globin insulin once daily, as Professor Dunlop says, is good for mild insulin cases—any type is almost equally good—but P. Z. insulin is probably better. But without full detail I merely want to record my opinion that one morning dose of globin insulin is a poor treatment for severe diabetics.—I am, etc.,

London, W.1. R. D. LAWRENCE.

Streptomycin and Insulin

SIR,—A patient who has both diabetes mellitus and pulmonary tuberculosis has made two comments on his streptomycin treatment: 1. While taking streptomycin (0.5 g. twice a day intramuscularly) his insulin requirements, to avoid glycosuria with the same diet, have increased from 55 or 60 units daily to 77 units daily. 2. Whenever he has injected ordinary insulin and streptomycin within an inch or two and within a few minutes of each other he has had severe pain between the sites of injection; but if kept further apart in time or in space neither is unduly painful. The severe pain is burning, "like a hot iron," and prevents sleep. One evening the streptomycin dissolved in 1.5 ml. of 1% procaine was given in proximity to insulin. The pain appeared, but not until about five hours later; and he had no more sleep that night. Publication of this may save others trouble pending further observations.—I am, etc.,

St. Leonards-on-Sea. E. A. WOOD.

Renal Complications in Diabetes Mellitus

SIR,—In their discussion of renal complications in diabetes mellitus in your issue of July 24 (p. 194) Drs. W. R. Gauld, A. L. Stalker, and A. Lyall make no mention of the condition of the renal arteries in their post-mortem cases. When an attempt is made to correlate hypertension with pathological changes in the kidneys the investigation has little value without a thorough examination of the renal arteries, in view of the work initiated by Goldblatt on the hypertension produced by ischaemia of functional renal tissue from constriction of the renal arteries. I have seen three cases of the syndrome which the writers describe, one in a young subject. While all showed conspicuous intercapillary glomerulosclerosis, this lesion was inconspicuous measured against the bore of the renal arteries, which in all cases was at some level reduced to a microscopic slit from severe atherosclerosis. There was also universal gross narrowing of the branches in the pelvis.

If a Goldblatt mechanism obtains in those cases, much more weight must be put on a lesion in the renal arteries than one at glomerular level. It is to be hoped that any future publication on the subject will give due prominence to this point. I have read some of the references which the authors cite. None mentioned the condition of the renal arteries.—I am, etc.,

Regina, Saskatchewan, Canada. NORMAN G. B. MCLETCHIE.

Diabetic Coma

SIR,—Professor D. M. Dunlop and Dr. J. B. Donald (Aug. 14, p. 352) are harsh in their criticism of Professor R. H. Micks's valuable article. The high death rate in the U.K. in cases of diabetic coma is attributable to the insufficient insulin dosage recommended in British textbooks. How many deaths has Professor Dunlop had in his last 54 cases of diabetic coma?

Surely no physician should treat diabetes without the facilities for blood sugar estimation? If he has not such facilities

and may have to treat the disease he should purchase the equipment and learn to use it. There is no room for lazy men in the treatment of diabetes.—I am, etc.,

Tel-el-Kebir, Egypt. D. HAMILTON, Capt., R.A.M.C.

Prevention of Dental Caries

SIR,—A masterly review of the distribution among the tribes and nations of the world of dental caries, and possible causes, by H. H. Neumann, of New York, was published last year as a letter in the *Lancet* (1947, **1**, 806). He concluded that "the factors commonly blamed, such as mineral deficiencies, fluorine deficiency, poor dental hygiene, inadequate sunshine, constitutional factors, vitamin deficiencies, and overuse of starch and sugar in the diet, have little effect on endemic dental decay, and do not explain the peculiar geographical distribution. The consistency of the food, the table manners of the people, and the extent to which cutlery is used are far more important. The disuse odontoporosis which leads to dental caries can be prevented and to some extent treated by restoring to the teeth their proper work of chewing . . . by adding sufficient toughage to what we eat." Earlier in the letter he suggests that "the addition of some hard breadcrust (old Swedish or Italian type of bread) to the daily diet would suffice to maintain fairly good teeth with a reasonable low caries incidence."

What a simple way of saving an enormous amount of suffering and waste of money on tooth-brushes and powders, stoppings, extractions, and artificial dentures. Teach, in the mothers' clinics, to use as little as possible cutlery and soft food and give children tough crusts to chew. Lady Mellanby has laid great stress on dietetic factors. Can she lend her authority to the spread of the use of toughage in the diet?—I am, etc.,

Smallfield, Surrey. LEONARD HILL.

Pioneers of Social Medicine

SIR,—Sir Arthur MacNalty's generous review of my Heath Clark Lectures (Sept. 4, p. 476) gives me an excuse for commenting on the publication itself. With rare exceptions, of which a course by a professor emeritus of epidemiology and vital statistics is not one, academic lectures do not pay the cost of publication. Sales merely slightly reduce the bill to be defrayed from trust funds. I should therefore have supposed that in these days of austerity it would have been sufficient to issue the lectures in paper wrappers and to put them on sale at less than the cost per copy of publication. That any member of the public, other than a lunatic at large, would be tempted by a green cover with gilt lettering and crest to pay 12s. 6d. for a booklet which can be read through in a couple of hours is, to me, incredible. However, the disgust with which I look at this ugly little trollop is partly due to injured vanity. Even medical statisticians *dream* of having readers other than personal friends.—I am, etc.,

Loughton, Essex. MAJOR GREENWOOD.

Genu Valgum

SIR,—In discussing the aetiology of genu valgum in Mr. H. A. Brittain's excellent article (Aug. 21, p. 385) omission is made of a simple mechanical observation. I have had opportunity of observing many infants who have developed knock knee as a direct sequel to tibial bow legs. Many babies have bow legs at birth due to a cramped position *in utero*, often an example of a large foetus in a small mother. If these cases are followed up during the first two years it will be found that as spontaneous correction of the bow legs takes place in the lower half of the tibial shafts the tibial arc straightens and the ankles diverge, resulting in genu valgum.

During the transition stage a familiar picture is seen comprising persistent femoral anteversion, genu valgum, slight tibial bowing, and an intoed gait. The intoeing is due to the combination of the femoral anteversion and the internal rotation of the tibial bow legs. With natural development the femoral anteversion and the tibial bowing are usually corrected, with resultant disappearance of the intoed gait. The residual deformity is now the knock knees, with prominent internal femoral condyles and widely separated malleoli. We must not assume that all children pass through the stages described, but careful follow-up from babyhood will show that it is not uncommon. This development I described in greater detail in *Physiotherapy* (June, 1948).—I am, etc.,

Birkenhead. HORACE DAVIES.

Reactions to Intravenous Sclerotics

SIR,—I should like to report the following acute allergic reactions following intravenous injection of venous sclerotics. I understand that such reactions are uncommon; out of many hundreds of injections of varicose veins by sodium morrhuate (usually 5%, occasionally 10%), I have seen only these two.

Case 1.—A man aged 64, nervous type and given to alcohol, was given 1.75-ml. doses of sodium morrhuate (5%) over a period of 14 months (1935–6). In 1943, owing to recurrence of the veins, he was given further injections of 5% sodium morrhuate as follows: Sept. 18, 2 × 1.75 ml.; Oct. 16, 2 × 1.75 ml. Half to one hour following the last injection he had the following symptoms: tingling of hands and feet, marked generalized itching, and collapse. This was regarded by me when reported as a nervous reaction aided by the fortification with alcohol before and after the injection, but he reported the same symptoms after the next injection. I therefore ceased using sodium morrhuate and gave him five subsequent injections, 3 ml. of 10% sodium salicylate, without any after-effect.

Case 2.—A man aged 48 was given 24 injections of sodium morrhuate. The first was of 2 × 1.75 ml. (5%), the subsequent ones being increased owing to the poor reaction to 2 × 1.25 ml. 10% sodium morrhuate. These were given over a period of three years. He was not a particularly nervous type, nor particularly given to alcohol.

At the 24th injection he had the following reaction: Within 10 minutes he complained of tingling and itching in the hands and genitals. This increased after he had gone half a mile, and the itching became general and intense. He collapsed about a mile away, fortunately outside the ambulance station. He was taken to hospital, where I saw him 50 minutes after the injection was given. He had an acute generalized urticarial rash. Pulse was good. He was given an injection of 0.4 ml. of liq. adrenaline hydrochlor., and in two hours he had recovered.

Fourteen days after this reaction he was given an intravenous injection of 4 ml. of 30% sodium salicylate and had a precisely similar allergic reaction, together with a feeling of swelling in the windpipe, this time in the consulting-room, where he had been kept. He was given the same treatment and he recovered in the same manner.

Acute allergic reactions following the intravenous injection of sodium morrhuate are uncommon. In the second case reported above the recurrence of an allergic reaction after changing to a completely dissimilar chemical substance must be even rarer.—I am, etc.,

Purley, Surrey. C. E. TAYLOR.

Fibrositis

SIR,—Surely the aetiology and pathology of fibrositis and its clinical manifestations were settled and agreed on long ago—since the days when Rabagliati termed it "perimyositis rheumatica," and Gowers gave it the name of "fibrositis," and Stockman, fully 50 years ago, expounded the whole matter, and demonstrated microscopically the lesions in the white fibrous tissue and how best to feel the nodules when the skin is lubricated with vaseline. But it is needless to say more. Thousands of doctors are satisfied, and have been for many years, as to what fibrositis is, its cause, its alleviation if not cure, and its treatment. It is an important and interesting subject, but a thing quite apart from the lesions of an intervertebral disk.—I am, etc.,

St. Andrews. R. O. ADAMSON.

Fibrositis and the Weather

SIR,—Whatever fibrositis is or is not, it is real enough to those who suffer from it. Many are able to tell with monotonous regularity when the weather is about to change for the worse. In Palestine, with its rapid succession of dry heat and damp cold in certain regions, it was common, often in the form of headache. The Arabs, who are presumably tough and uninhibited, would often ask for aspirin for this condition.

The point has been raised before, but I still do not know, and no pathologist has told me, why an old wound aches in damp weather. I have often thought that the fibrositic tissue was in some way structurally impaired, similarly to scar tissue. If the effects of weather are so striking in this condition it

should not be difficult to experiment with fibrositic subjects in artificial climates. At the risk of being tedious I suggest that the effects are not due entirely to temperature, pressure, or humidity, but that the electrical changes in the air should also be considered.

The awareness of temperature and climatic changes seems to vary much from one person to another. Some quite suddenly discover that they are much too hot or chilled right through. In my student days I sometimes started work in a warm room, to be discovered by a relative some hours later chilled right through, with the fire out, and quite unaware that this had happened until I was bundled into bed and warmed up. I cannot concentrate so well now.—I am, etc.,

Hadley Wood, Herts. G. C. PETHER.

Cerebral Aneurysm

SIR,—Cases of ruptured cerebral aneurysm are, one understands, by no means rare, yet sufficiently so that I do not recollect in 20-odd years of practice being reasonably convinced of being in the presence of one. Nevertheless I have lately seen two which were confirmed at necropsy. Both were men about 30, both had recently been discharged from the Forces, one having seen active service in the Tank Corps and the other in the Infantry, which prompts one to speculate how far the vigorous training called for in both these units led to these aneurysms bursting when they did, and causing one to wonder why, under the stress and strain of training and active service, they did not do so before.

I was called out at midnight to the first case and found him in bed complaining of the sudden onset of violent occipital headache and of loss of power in his legs. He had also been sick. He felt rather better next morning and had regained the use of his legs, but the headache persisted. B.P. was normal, Kernig's sign was positive, and there was some nuchal rigidity. He survived two or three weeks in hospital, but eventually succumbed. His wife informed me that his original attack had come on during sexual excitement.

In the second case the patient had on the previous evening been to a regimental reunion and had collapsed in the street just after leaving. He admitted that he took "a few beers," but denied any excess of conviviality. He also complained later of occipital headache and vomiting, and within a day or two he had a positive Kernig's sign and nuchal stiffness. He refused to go to hospital and was away from work for six to eight weeks, when he returned to work apparently quite well. One morning about four months later, just as he was cycling past a hospital on his way to work, he collapsed off his cycle and was already dead when picked up or died shortly after being admitted.

As stated above, post-mortem examination confirmed the presence of ruptured cerebral aneurysm in both these cases.—I am, etc.,

Hove. G. L. DAVIES.

Shipping the Sick

SIR,—Shipping of the sick on a British ship is a nightmare. May I give this example? I managed to send a girl missionary to England—? tuberculous caecum (two outside surgical opinions)—for domestic, financial, and climatic reasons. I might have been trying to send a case of plague home. I gave full case notes, chest radiograph, sputum reports, and the almost certain guarantee that she would require no medical attention. Finally, when I was lucky enough to guarantee that if she required medical attention there was a missionary doctor on board who would take full responsibility, she was accepted with bad grace. Comparisons are odious, but the difference on American ships is astonishing. Friendliness, delight at receiving case notes, and willingness to accept responsibility have been my experience. Unfortunately these ships do not use British ports.

If shipping companies want "protection," it should be possible to have a medical board to decide the suitability and circumstances of a patient to be sent home. The laity of the shipping companies cause the initial obstruction. And again I know of cases where the doctor has not disclosed that the patient has been ill—in the patient's interest—and they have gone as ordinary travellers. Personally I am nervous of taking any risk and prefer to face the music; and have the remark, as in the above case, "I'm not having shore doctors push their responsibilities on to me."

British men and women abroad should be entitled to expert opinion and treatment in their home country if thought advisable, and the courteous and correct handing over of a case history should not be considered as a "shifting of responsibility."—I am, etc.,

Colombo. B. M. NEWEY.

Stainless Steel Wire

SIR,—I was most interested in the paper by Messrs. A. Lawrence Abel and Alan H. Hunt (Aug. 21, p. 379) and should like to add a few observations in support of this excellent suture material. Two years ago Mr. Alan Hunt initiated me into the use of stainless steel wire, and I have employed this suture for every abdominal section since. The unverified total is between five and six hundred cases, and I have nothing but praise for stainless steel wire.

In a Hunterian lecture recently published in the *Lancet* (July 17, p. 85) I drew attention to the importance of early ambulation in the avoidance of post-operative complications. There is no doubt that stainless steel wire enhances the confidence of a surgeon and his team in getting patients out of bed the day after operation. Nothing but good has accrued from this, and the incidence of fatal pulmonary embolism in my cases in the last two years has been one case. This occurred in a woman who had multiple abdominal sinuses following an operation some two years previously and in whom the ultimate diagnosis was actinomycosis. It was interesting to note that she was too ill to be given ambulant treatment after operation, and a post-mortem examination demonstrated a large clot in the pulmonary artery arising from the internal iliac veins, presumably of septic origin. There have, however, been a number of cases of leg thrombosis and/or pulmonary infarction successfully treated by heparin, in spite of early ambulation. This is mentioned because early ambulation, though helpful, is not the final answer in the prevention of phlebo-thrombosis and thrombo-phlebitis.

The test case for stainless steel wire was a recent one in which a straightforward total hysterectomy was followed by paralytic ileus. The patient's abdomen was enormously distended for 10 days, and the suture line was put to a test which I feel sure that no other material than stainless steel would have withstood. Any surgeon who uses catgut must sooner or later have a burst abdomen, no matter how carefully he ties his knots or spaces his interrupted sutures. In 1944 I performed a myomectomy on a member of the W.A.A.F. and sewed the rectus sheath with interrupted catgut. For no reason at all she burst her abdomen on the fourth day, and examination of the suture line revealed a necrosis of the sutures, which were incompetent to hold the tissues in place. Such a case is unlikely to occur with stainless steel wire when properly employed. On one occasion my wound has been taken down by another surgeon for an acute appendicitis developing some weeks after hysterectomy. He reported a sound, clean, first-intention healing of the original incision.

I have been asked on many occasions what would happen to the stainless steel sutures if the patient were to receive diathermy treatment or *x*-radiation. This is a question that ought to be answered.

Finally, I can only say that since I have employed stainless steel wire the instance of wound sepsis has decreased almost to vanishing point, and that any sepsis which has occurred I think can be fairly blamed upon the use of catgut to tie subcutaneous bleeding points.—I am, etc.,

London, W.1. JOHN HOWKINS.

Prevention of Venereal Disease

SIR,—I have only just seen the *Journal* of Aug. 21, and the letters (p. 400) from Drs. W. B. Laing and F. R. Curtis commenting on mine in your issues of July 31 (p. 269) and Aug. 7 (p. 313). May I reply in one letter?

The fact of the existence of V.D. is a side issue to the main problem. If this disease could be entirely removed, or an infection immediately cured, a devastating illness would be thankfully banished. But if injustice, exploitation, disloyalty, and unchastity remain in the relation of individual human being

to one another, or in the relation of State and people, the root of mental and bodily ill still exists. Countries which have practised that State regulation of prostitution recommended for our adoption by Dr. Laing have turned from it not only because its uselessness in controlling V.D. is apparent but because the proved results—degradation of men and women, and especially of youth; appalling injustice; the tentacles of vested interests; the traffic in women and children; the militancy of the whole system against justice and love—have finally revolted the human spirit.

The scope of law should be strictly limited, especially in relation to sexual morality. But there is a tendency to-day in every country and in every political party to formulate legislation on what seems expediency rather than on strict principle. Then very soon laws are made which apply to particular classes of persons only; regulations which no one can keep track of undermine rather than clarify law; and the power of the executive continues to grow.

I know enough of the work of V.D. and other clinics to appreciate and respect the enormous care that has always been taken to attract and retain the confidence of sick persons. I know also that the medical profession does not need legal sanctions to force it to keep the confidence reposed in it. Whatever the law, or lack of it, as I said in my previous letter, no doubt all concerned with V.D. patients will do all in their power to maintain confidence and keep information confidential. But with the removal of the statutory requirement of confidence they may not be able to do so. Even with this requirement a doctor can be called to give such evidence in a court of law, but this is very rarely done. The power to keep medical information confidential seems to be rapidly going in this country, as Sir Ernest Graham-Little has pointed out, and it has gone in some countries.

Under Defence Regulation 33B the legal requirement of confidence ceased to apply with regard to certain persons known or alleged to have V.D. I did not hear that any member of the medical profession objected to giving evidence or to sending his medical reports on such V.D. patients, whose confidence, presumably, was as worthy of respect as that of any other patient. The law allowed and required such information, and it was given. If the law allows breach of medical confidence in relation to V.D. patients at public clinics, as it now does, it will in a very short time *require* it for certain classes of persons, and the medical and allied professions will be in a very difficult position. The patient loses not only some guarantee of medical confidence but also a very real protection against the casual or malicious gossip of acquaintances.

The World Health Organization has plans for various World Conventions relating to health and disease. There is much that is good and necessary in these proposals, though the tendency to mass compulsion of all sorts is apparent. Certain of the V.D. proposals, particularly, seem to be in many respects dangerous to justice and liberty. They provide for an international "black list" of certain defaulters, compulsory hospital detention, investigation of suspected or alleged sources of infection, and so on. The past and present history of such attempts, on a smaller scale, shows that officials (medical and police) are thus given almost unlimited power over certain individuals known, suspected, or informed against, or whose alleged way of life suggests that V.D. may be present. Very little thought is needed to appreciate the acute danger of such power, both to those who have it and those who have to submit to it, or to see that "confidence" must be non-existent in such proposals.

The World Health Organization has unique power, in that any resolutions it may adopt come automatically into force for all member States unless objection is registered within a certain period. My Association considers that the public should know as much as possible about the national and international legislation to which it is, or is being, committed. With regard to V.D., for instance, why should the public be misled by the Minister's continuing propaganda and advertisements guaranteeing secrecy and confidence? It cannot now be guaranteed, however much the staffs of the public clinics may and do desire to keep that confidence. A test case is bound to arise, and then it will be known if, in Dr. Curtis's words, "secrecy is now so strongly entrenched by custom in the minds of the public and clinic staffs that a statute is unnecessary to buttress it."

Many people in every country are appalled by the denial and disintegration of justice and of individual freedom. It is this Association's business to seek to know and to fight for justice in its own specialized but fundamental work, and that it is doing.—I am, etc.,

KATHARINE B. HARDWICK,
General Secretary,
The Association for Moral and Social Hygiene.

London, S.W.1

SIR,—All your correspondents on both sides err in regarding venereal disease as a moral problem. Venereal disease is a social problem. It is caused by the failure of so-called civilized society to settle its problems other than by war, to pay its young people a wage adequate to enable them to marry at the physiological age for marriage, child-bearing, and parenthood, and to provide its young people with homes for themselves and their children.

If a young man is doing a job which is necessary to the community he is entitled to the wage and to the house which will enable him to support a wife and family. Without his children to carry on his job when he is done society will not survive.

Attempts to prevent venereal disease by continence or by condoms are alike futile and the result of muddled thinking. Like all therapeutic measures they do nothing to remove the cause of the problem and so do nothing to prevent its perpetuation.—I am, etc.,

Tavistock, Devon. JOHN SLEIGH.

SIR,—This hoary quinquennial is always productive of the larger prejudices, moral, medical, social, humanitarian, and religious, but in the interests of accuracy the more extreme examples cannot be allowed to pass unchallenged.

That provision and knowledge of prophylaxis, control, or other measures increase or decrease promiscuity and/or numbers of infections is admittedly debatable, but to affirm, as does Dr. R. C. Webster (Sept. 4, p. 499), that "there is no method of prophylaxis which affords any significant degree of protection" is contrary to all accepted evidence. The 1922 Trevethin Committee's findings on this point have never been seriously challenged.

It all depends on what is considered significant, but that the medical and general staffs of all the Allied Forces would have permitted a not inconsiderable portion of their manpower, preventive organization, accommodation, and equipment in every theatre on land and sea throughout the war and after to have been wantonly wasted in a futile endeavour seems, to say the least of it, somewhat improbable. Venereologists are truly "incredulous," not least of alleged use of P.A.C.s, etc., by their patients.

That closure of brothels in Cairo and elsewhere resulted in a diminution in the incidence of disease is an accepted fact. The old B.A.O.R., in which I had the fortune to serve i/c the Connaught Hospital, Wiesbaden, in 1927 and 1928, and the French Army in 1930 somewhat to its surprise, made the same observation, the latter over an experimental year in a typical garrison city, Metz. (It should always be remembered that peacetime conditions are not comparable with war.)

To allege, however, that supervision, where it existed, was everywhere cursory and futile is an exaggeration. Such control could and did eliminate the grosser macroscopic, sometimes condylomatous, varieties of disease, and where conscientiously exercised, as it was within the observation of venereologists in many areas of the B.E.F. in 1939 and 1940 by the French Army and civilian medical services, was a great deal better than none at all, and to its efficacy may be attributed at least in part the relatively low incidence of disease in the B.E.F.

Most will agree with Dr. Robert Forgan's (July 31, p. 269) melancholy reflection, and will regret that so far from having any further powers, so cogently demanded by Dr. Laird recently, even the timid wartime advance of 33B has now been withdrawn.—I am, etc.,

London, S.W.1. W. H. DICKINSON PRIEST.

SIR,—Colonel P. F. Chapman (Sept. 4, p. 498) asks how I protect my hands against infection in examining venereal patients. The answer is obvious: by using rubber gloves and/or antiseptics. As adults we are aware that there are certain differences between the conditions of professional examination and coitus. The contacts of examination are brief; the examiner is presumably sober and is not excited;

he exposes certain defined areas, and has technical skill in the removal of his gloves, which protect a wide margin about his fingers. In coitus the exposure is to relatively prolonged frictional contact under pressure; the areas involved are freely secreting; the individual is emotional and not necessarily sober; and if chemicals are used they are applied at an indeterminate later time. A condom protects a very limited area: chancres of the root of the penis or the scrotum are not rare.

The question whether an effective method would be opposed on moral grounds is irrelevant—we are asking if such a method does in fact exist. If the application of calomel cream after coitus would prevent syphilis I do not see that it has any moral bearing. That is a non-specialist opinion, and as such of little more or less value than my views on mathematics. Similarly Colonel Chapman's statements in his letter on morals generally and on social anthropology of sex have no special value other than as individual opinions. They have no value in deciding whether effective prophylaxis of venereal diseases is possible.

In fact, as distinct from theory, I know that elaborate plans for prophylaxis in the Services were a failure. I have visited many prophylactic centres, seen the busy traffic of issuing outfits, and like any other venereologist heard all the tales that begin, "It can't be that, I used . . ." To the enthusiasts I would say, Ponder a little on the mechanics of coitus, and add to the result of these meditations common-sense knowledge of the actual circumstances of promiscuity, physical and mental, and it will be clear that prophylaxis is not practicable. —I am, etc.,

Todmorden, Lancs R. C. WEBSTER.

SIR,—Dr. R. C. Webster (Sept. 4, p. 499) suggests that "the views of a doctor in his *professional* capacity as to the value of marriage certificates and chastity as an ideal have no special value." I wish to make it clear that I entered into this correspondence principally to protest at the introduction of the question of morality by Dr. G. L. Russell (July 31, p. 268), and to reject as of no practical value Miss K. B. Hardwick's platitude (p. 269) that "the only sure prevention of V.D. is chaste living . . ."

The figures provided by Dr. A. Michael Critchley (Sept. 4, p. 499) illustrate the value of controlled brothels in Egypt. When the Cairo brothels were in bounds there is no doubt that the majority of exposures to infection occurred there, yet only 52% of the V.D. cases were infected in this way. That the number of men having intercourse outside of brothels was small is confirmed by the drop in the apparent exposure rate to one-tenth which followed their being put out of bounds. The corresponding fall in incidence of V.D., however, was only one-quarter. From these figures it is obvious that in the Cairo area it was very much safer to have intercourse in a controlled brothel than elsewhere.

I object, however, to the assumption that Egypt provides a satisfactory example of the controlled brothel. Doubtless an attempt to enforce chastity in military personnel will have a certain degree of success in the prevention of V.D. in countries like Egypt where, by putting certain areas out of bounds, the opportunity for promiscuity is reduced almost to nil, but I think Dr. Critchley is wrong in attributing the drop in promiscuity, and especially the improvement in "the general conduct, morals, and morale of the troops," entirely to the fact that in October, 1942, the brothels in Cairo were put out of bounds. The victory at El Alamein (October, 1942) and the glorious advance of the 8th Army which followed should, I feel, be given some of the credit.—I am, etc.,

Edinburgh. W. B. LAING.

SIR,—The recent series of letters on this subject has been a source of considerable interest, if only to observe the generations-old conflict of ideas voiced again in yet another form: abstinence *v.* biological urge, prophylaxis and education *v.* increased promiscuity, the licensing and medical inspection of brothels *v.* their increased use and subsequent suppression, sympathy *v.* punishment for the sufferers, and notification *v.* the liberty of the subject are the basic chords, but the whole has become hopelessly entangled and indeed has always been so. The tragic part of the whole business is that so diverse are the views which are so sincerely held by their proponents we appear to have a number of agencies all professing to work to the same ends yet quite unable even to consider working together. As a result nothing really worth while is done and we muddle on as before.

A study of the issues involved leads at any rate to one inescapable conclusion which, once realized, holds out real hope for the future. That is that case-finding is the only *essential* for venereal disease prevention. If all persons infected with venereal diseases were placed under treatment it would not matter in the slightest how monastic or promiscuous persons were, or how hygienic or otherwise their sexual behaviour. Neither, strictly from the V.D. standpoint, would it matter whether brothels in any form existed or not, or whether or no troops should be discouraged from visiting them. Granted this thesis—that case-finding is the kernel of the problem—here is the common denominator for the agenda of the National Society for the Prevention of Venereal Disease, the Association for Moral and Social Hygiene, the Central Council for Health Education, and all similar bodies interested in these diseases, not to forget the Ministry of Health and the doctors working in the clinics.

Here then is the means—for the necessity of case-finding cannot be gainsaid. The members of all the above bodies must unite on this to solve the one remaining conflict, that of notification *v.* personal liberty; and in this will be found scope for all to produce a formula which is satisfactory to the British way of life. The thought of notification and a "venereal police" is quite abhorrent to the majority, but existing methods are inadequate for their purpose. The contact slip as used in the clinics achieves some success for known contacts, but what, if anything, should be done, either individually or collectively, for those that are unknown is the real crux of the matter and deserves the attention of all. Let case-finding be the number one aim, but at the same time the propaganda of these societies and bodies should still preach their favourite subsidiary methods. As long as these are kept subservient to the main issue there can be no great disharmony.

In order to quell any criticism that it is easy to write generalizations I will conclude with a practical suggestion. In recent years propaganda trains, such as the penicillin train and the atomic energy train, have toured the railway stations of the country. Let the above-mentioned educational bodies together sponsor a V.D. train, with the accent on case-finding. Within it the individual factions can each also advocate their chosen auxiliary measures.

I apologize, Sir, for coming in at the end of what is now a very lengthy correspondence, but hope you will permit this contribution to be published before blowing the final whistle. —I am, etc.,

London, W.2. R. R. WILLCOX.

*** This correspondence is now closed.—ED., *B.M.J.*

Shortage of Nurses

SIR,—Dr. N. Strang, in his recommendations (Sept. 4, p. 500) for nursing recruitment, has placed in a nutshell what the Working Party has failed to do in a volume. May I add that not only should the student nurse be given a professional salary on qualification but that during her training she should be given the same status as any other university student. To suggest that inflexible rules and regulations, still so prevalent to-day, are necessary for hospital discipline does, in my opinion, reflect darkly on the ability of those charged to maintain it.

If the same methods are used to attempt to attract girls to the nursing profession as are regularly used to draw them to under-manned industries, then it seems to me that those qualities of initiative and responsibility—the hall-mark of any profession—will gradually disappear from the nurse as they have done from the industrial worker since the standard methods of recruitment were started at the time of the Industrial Revolution. —I am, etc.,

Birmingham. JAMES R. CROSS.

SIR,—Dr. N. Strang's programme (Sept. 4, p. 500) for dealing with the chief menace in the hospital world to-day is refreshingly constructive. It omits, however, practical suggestions for dealing with a major cause of reluctance to enter the nursing life—viz., the attitude of parents who become experts in steering their girls to other channels of employment, not without reason, though their thoughts are often camouflaged. They are conscious of the too high sickness rate that is common during training years. This factor in shortage has never received due attention.

Even this year a young nurse in a London teaching hospital can lie in a sick-bay for some eight weeks with no care at a higher level than that of a young R.M.O. who tells the parents not to fuss as all tests are negative. When at last "convalescence" is arranged and three weeks at the sea are over the girl can return to duty and be put on "night" with no further investigation. Further breakdowns need surprise no one. Such handling of nurses' health is not good propaganda, but it seems nobody's business to raise the general standard of care for the rare and precious human material that our hospitals lack.—I am, etc.,

Northwood, Middlesex. ESTHER CARLING.

POINTS FROM LETTERS

Low Back Pain

Dr. F. W. INMAN (Wallasey) writes: In my time low back pain has been consistently called lumbago, and has been blamed on the liver not turning uric acid into urea. The treatment has been always by large doses of salicylates and colchicum. With experience in a busy surgery extending over fifty years I have found this treatment sufficient in most cases. True there are residual cases, which can be recognized by their failure to respond, but these are a comparative rarity and no doubt should be investigated with a view to surgical treatment. In the old days when gout was more often seen the connexion with severe lumbago would be more easily recognized. In one of his books Dr. Thomas Inman, of the old Royal Infirmary, Liverpool, gives a most graphic account of an attack. As port medical officer he had been on board a ship in the Mersey and had strained his back getting on board. Whilst being rowed back to the landing stage he took an opium pill, and the coxswain read the label. Climbing up the rope ladder he cricked his back again and had to be helped up. On the stage he was unable to speak, and the men, at the direction of the coxswain, ran him up and down the stage thinking that he was suffering from opium poisoning. . . .

Dangerous Talc

A correspondent writes: I was interested to read in the article in the *Journal* of June 5 (p. 1077, *et seq.*) and in the annotation on page 1090 that it has been discovered that talc can cause granulomata. Not so many years ago I was lying in a sanatorium bed suffering from pulmonary tuberculosis, and every day I was religiously washed, rubbed with spirit, and dusted with scented talcum powder. I remember wondering at the time whether talcum powder was likely to cause silicosis, because every time I turned over in bed I inhaled a shower of it, blown up from between the sheets. I used to console myself with the thought that the Superintendent would not have allowed its use if it had been harmful. What simple faith one had in those days! However, I made an uneventful recovery in spite of the talc. But in view of these recent disclosures I think doctors might well discourage its indiscriminate use by enthusiastic nurses, especially where such a delicate thing as a tuberculous lung is concerned.

Fourth Attack of Mumps

Dr. W. W. NEWTON (Birmingham) writes: I have seen a young woman aged 17½ years in my surgery this morning with a swollen and tender left parotid gland and general headaches and malaise. Her temperature was normal. In May, 1946, she had typical mumps, and also twice in childhood during school attendance. To have mumps four times in about 12 years is surely very unusual and worth reporting.

Spraying Fruit

Dr. JAMES FORREST (London, W.1) writes: Always partial to raw and cooked fruit, I ate my first basket of strawberries with relish, but an hour later I was overcome by a feeling of nausea so strange as to be mystifying. Not until a fortnight later did I eat other strawberries which occasioned a nausea that three hours later was followed by vomiting so violent and instantaneous that before I could reach the lavatory my stomach emptied itself. Assuming that the reaction was a recent allergy it was without apprehension that I ate red currants and raspberries, but similar symptoms were induced and suggested that some poison introduced by spraying the trees or the fruit after it was picked was responsible, which was confirmed by the fact that from a garden in which no chemical is used I ate similar fruit in large quantities without the slightest ill effect. So prevalent are gastric disturbances this summer that, according to the Press, some councils have issued circulars warning the public against consuming fruit or vegetables that have not been thoroughly washed. But more informative and more valuable would be the opinion of general practitioners upon a subject that is so far-reaching in its significance.

Obituary

S. W. WHEATON, M.D., F.R.C.P.

Dr. Samuel Walton Wheaton, a former medical officer of the Ministry of Health, died on Sept. 5 at the age of 86. He was born in Salisbury in 1861, and received his medical education at St. Thomas's Hospital, where he held appointments as house-physician, resident accoucheur, and as demonstrator of physics. Before becoming a medical student he had acted as personal secretary to Sir Henry Fawcett, the blind Postmaster-General, and he continued these duties while a student, frequently studying for long hours at the House before taking Sir Henry back to his home near Vauxhall after late night sittings. Nevertheless he won the Mead Medal for Practical Medicine and gained a *proxime accessit* in the Murchison Scholarship.

Dr. Wheaton qualified in 1886, obtained the London M.B. with honours in medicine and forensic medicine in 1887, and proceeded M.D. in 1888. He took the D.P.H. of the English Conjoint Board in 1889, was admitted M.R.C.P. in the same year, and elected F.R.C.P. in 1906. He was a councillor of the Royal College of Physicians from 1926 to 1928. Early in his career his interests lay in diseases of women, and he obtained the post of physician to the Royal Waterloo Hospital for Women and Children, and contributed articles on obstetrics and gynaecology to clinical societies and medical journals. He maintained this interest throughout his long life, contributing a chapter on maternity and infant welfare centres to the *Practitioner's Encyclopaedia of Midwifery and Diseases of Women*, which was published in 1921.

At the end of the last century Dr. Wheaton gave up his hospital appointments and became a full-time member of the public health service, first as an inspector of the old Local Government Board and later as a medical officer of the Ministry of Health on its formation. He was a member of the Epidemiological Society before its fusion with other societies to form the Royal Society of Medicine. He served as medical assessor to the Miners' Welfare Committee and took an active interest in, for example, the provision of pithead baths. For more than thirty years Dr. Wheaton was engaged in Governmental inspections and inquiries directed to the control of epidemics and to the improvement of local public health administration, claiming to have visited nearly every village in Wales on foot in connexion with his work. More than twenty of his official reports have been published.

He was a keen naturalist, with a great interest in geology in its relation to water supplies. Painting was his lifelong hobby, and he had considerable skill, his colour sense being developed to an unusual degree. He never failed to bring back from his tours of inspection a number of watercolour sketches, later to be interpreted in oils. He exhibited frequently in the exhibitions organized by the Ministry of Health and other civil service art clubs and associations. Dr. Wheaton retired from the Ministry of Health in 1927, but was extremely active to within a few days of his death. His two sons are both members of the medical profession.

Dr. J. Alison Glover writes: Greatly to my advantage I shared a room with Dr. Wheaton for the last six years of his official career. He was one of the great age of Victorian sanitary reformers, retaining alike the side-whiskers and the morning tail coat of that era, and might have passed for the typical father of 1900. Before I knew him I thought his appearance formidable, but he proved invariably kind. He was a great pedestrian, walking to the office and back daily from Streatham Hill, and his unrivalled acquaintance with the details of the sanitary circumstances of this country was due not only to his retentive memory, keen observation, and long experience but especially to his rule of making all his inspections on foot. He seemed to have walked over every rural district in Britain. He was a competent geologist, and his knowledge of almost every gathering ground had a lasting influence on the policy guiding the water supply of this country with its particular emphasis on the purity of the source, an emphasis which has been wholly beneficial. By the time I knew him his views were naturally somewhat conservative, but to the last he was always

ready to adopt well-proven new methods, and he had been an early pioneer in the introduction of the maternity and child welfare service. On by-laws, particularly those relating to conservancy, nuisances, and offensive trades, his was the final opinion. I shall not forget the impression he made upon a deputation from the Ministry of Health of Czechoslovakia which visited this country soon after the first world war. It was my duty to conduct them during their visit, when they met many of the prominent public health authorities. None impressed them more than Dr. Wheaton, with whom they were frankly delighted. Dr. Wheaton's death removes one of the last of the great environmental reformers, whose valuable services to his country have scarcely received the recognition they deserve.

A. W. GILL, M.D., F.R.C.P.

Dr. A. Wilson Gill, one of the leading members of the profession in North Staffordshire, died in the North Staffordshire Royal Infirmary at the age of 60 on Aug. 30. Alexander Wilson Gill, a native of Edinburgh, was educated at the Royal High School there and at Edinburgh University, where he graduated in 1909. After qualifying, Dr. Wilson Gill became a house-surgeon and later house-physician at Addenbrooke's Hospital, Cambridge, and subsequently resident medical officer at the City Infirmary, Birmingham. In 1912 he proceeded M.D., his thesis being on the study of auricular fibrillation using electrocardiographic methods, which were still in the early stages of their development. In the same year he went into general practice as an assistant to the late Mr. Reginald Alcock at Hanley and subsequently was in partnership. During the 1914–18 war Dr. Wilson Gill was in charge of the medical arrangements at a poison gas factory for two years before being commissioned in the R.A.M.C. and serving in France and Belgium with the 53rd Field Ambulance. In the closing stages of the war he was regimental medical officer to the 6th battalion of the Dorsetshire Regiment. During the war Dr. Wilson Gill became increasingly interested in neurological problems. He experimented with hypnotherapy, and subsequently published a number of papers on the problems of neurosis. At the same time he maintained his interest in cardiology and took charge of the cardiographic department of the North Staffordshire Royal Infirmary. His connexion with the infirmary began with his appointment as an honorary medical registrar there, and not long afterwards he became one of the assistant physicians and later physician to the hospital. He also served on the honorary staff of the Burslem Haywood Hospital and for a period of eight years the Staffordshire General Hospital. Until the time of his retirement he was in charge of both the neurological and cardiological departments of the North Staffordshire Royal Infirmary. He took the M.R.C.P. in 1927 and was elected F.R.C.P. in 1944, by which time he had been in consulting practice for some ten years. He was at one time president of the North Staffordshire Medical Society, and was president of the Staffordshire Branch of the British Medical Association in 1935–6. As a young man he was a keen tennis player, and later in life he fished for trout regularly in the River Dove. The sympathy of his many friends and colleagues will be extended to his widow, formerly Miss Edith Mary Johnson, of Congleton.

THOMAS GWYNNE MAITLAND, M.D., D.Phil.

Dr. J. C. Matthews writes: The obituary notice of Gwynne Maitland (Aug. 28, p. 445) revived my memory of my first meeting with him in a B.M.A. committee-room in the middle 'twenties. It is of a courteous English gentleman with an encyclopaedic knowledge of affairs in general and of all branches of medicine in particular. He was already the much-valued medical superintendent of the Cunard Line, and we met as members of an *ad hoc* committee appointed to consider the status and training of the ship doctor; Courtenay Lord was secretary to the committee. At that time Maitland was *au fait* with all the problems; his own company and several others had already instituted very necessary reforms, leading to the establishment of a definite and worthy branch of the profession. His contribution to the work of the committee was therefore outstanding. I have not seen Maitland during the war years; previously we met from time to time, usually on trains, and his wide interests made him a delightful travelling companion.

Dr. Fergus Armstrong writes: Dr. Gwynne Maitland was known to many doctors for his genial personality and great help in transatlantic voyages. For five voyages he was surgeon in the *Franconia* for the cruise round the world, and in America he was truly a real British ambassador. Thousands of Americans who voyaged with him found him a great gentleman, and always spoke of him in the highest terms. Deck tennis owes him its first rules, and he was an excellent exponent of lawn tennis and deck tennis. I first met him in 1915 when he was medical director of Lady Paget's Hospital of the Serbian Relief Fund in Serbia. He surrendered the hospital to the Bulgarians and was a prisoner of war for six months in Serbia with our unit. In those days he was the life and soul of the hospital and kept all our spirits up during those trying days. Medical travellers across the Atlantic will miss his guidance, for he was a great help to all the profession who went to America.

Dr. STANLEY DUNN METCALFE, who died in May this year at his home in Newcastle-upon-Tyne, aged 63, was born in Sunderland and trained at the Durham College of Medicine, graduating M.B., B.S. in 1907. After serving as junior and senior house-physician in the Royal Victoria Infirmary, Newcastle-upon-Tyne, he became assistant to the late Dr. Neil Maclay at Wallsend for some two years. He spent the next eighteen years in general practice in Newcastle, after which he became a regional medical officer with the Ministry of Health. In that capacity he worked in Middlesbrough, Preston, Darlington, and finally in Newcastle. In 1946 he suffered from a coronary thrombosis but was able to resume his duties, and he carried on until the day of his death from a further thrombosis. A man of retiring habits and high ideals, Dr. Metcalfe was beloved by his patients, whom he served so well. An omnivorous reader, his chief interest was in archaeology; his holidays were spent in visiting cathedrals and churches in Britain. To those who had the privilege of knowing Metcalfe in his home life his loss comes as a heavy blow. For it was especially there that his quiet and sound philosophy was most apparent, and it was there that his valuable advice, culled from his vast store of human experience and understanding, was so readily available to all who sought it. Many young students and professional men will have in their minds a picture of Metcalfe sitting in his chair against the background of the books he loved, and will recall the memory of one who enjoyed life in his own quiet way and gave of his best to others.

Dr. HENRY FRANCIS BELL-WALKER died in July at his home in Cape Colony at the age of 72. Entering Guy's Hospital with a scholarship and graduating in 1903, he proceeded M.D. three years later. He was successively clinical assistant and medical registrar at Guy's Hospital, resigning the latter appointment in 1907 to go to South Africa to a practice at Bedford. He served with the S.A.M.C. in the first world war and went through the South West African Campaign, during which time he wrote *A Doctor's Diary in Damaraland*. In 1931 he left Bedford and went to farm in the Kat River valley, but still found time to practise medicine among the natives and poorer people of the district. Throughout his farming life he kept in close touch with his profession and in 1938 was awarded the Hamilton-Maynard Medal for his article on the prognosis of heart disease, which was published in the *South African Medical Journal*. He was a member of the Medical Council for five years, and, being particularly interested in medical education, was appointed an examiner. He again served with the S.A.M.C. from 1941–5, and was appointed physician specialist at the Military Hospital, Durban. Latterly Henry Bell-Walker became convinced of man's dependence upon the soil and of the impossibility of building a sound civilization without true husbandry. Briefly his articles of faith were: "There is no life without food or food without life. There is no health without good food. There is no good food except from good earth. There is no good earth without good care. There is no good care but what you give yourself." And it is as he was in this last phase of his long life that those who knew him best will always remember him.

Dr. EMRYS DANIEL OWEN died at Swansea Hospital on July 21 at the age of 50. He had been engaged in general practice at Neath for the last twenty-two years. Emrys Owen entered Aberystwyth University in 1916 after winning the premier entrance scholarship. After two terms he was called up, and spent two years in the Army and Flying Corps. From

1919 he continued his medical studies at the Welsh School of Medicine in Cardiff, taking the B.Sc. in 1921. He completed his medical training in 1923, and was one of the first four students to qualify from the Cardiff Royal Infirmary, which had by then been recognized as the parent hospital of the Welsh School of Medicine. His career at Cardiff was a distinguished one. He gained the Alfred Hughes gold medal in anatomy, and the gold medal in obstetrics and gynaecology. He held several resident appointments at the Royal Infirmary, and the surprising thing is that he did not continue in hospital work; his record and abilities were such as to assure him a future as a consultant on the staff of the hospital. He chose, however, to go into general practice, first as an assistant in Maesteg and then at Neath, where he spent the happiest years of his life, being loved not only by his family but by all his friends and patients. Emrys Owen was a good doctor and an outstanding personality. He was always so humble, and those of us who realized his capacity appreciated his unostentatious ways and manner of expression. He was an active member of the executive branch of the Swansea Division of the B.M.A., a member of the local medical committee for Glamorgan, and a past president of the Neath Rotary Club. He was a founder member of the Neath Medical Society, and just before his death he was appointed to the West Glamorgan Hospital Management Committee. His death has meant a great loss to the profession, and above all to his widow and two young sons, to whom the sympathy of all his colleagues will be extended.—R. D. O.

Dr. DAVID ALEXANDER MURRAY, who died suddenly on Aug. 9 while on holiday at Dornoch, his birthplace, will be sadly missed both in his native Sutherlandshire and by his patients and friends in Helmsley, where he had practised for many years. He graduated at Edinburgh University in 1925, but before even matriculating he had during the 1914–18 war the unusual experience of leaving school and getting to the French front. He was still so young that when the authorities noticed his age he was sent home to start school again. He was one of the best of country doctors, with a good knowledge in medicine applied with much common sense. He knew the family and background of each patient, and every one of them he treated as a friend. When winter in the dales was too severe for normal transport he would set off cheerfully by tractor, sledge, or on foot. His main recreations were racing and golf. At the former he declared he was always in the end successful as a punter; at the latter there was no doubt about his excellence. He learned his golf in his native Dornoch, and there are many stories of his battles royal with champions visiting there, battles in which he by no means came off worst. His friends will miss greatly his cheerful good humour and his unselfish ways. It is difficult to think that we will not meet him again by the bedside or on the links, and that affectionate memories are all that remain.—D. R. C.

Dr. ONG CHONG KENG was murdered on the evening of Aug. 31 while answering a call to attend a sick person. Dr. Ong was one of the most prominent members of the medical profession in Penang. He was born there in 1904, and was educated at the Penang Free School. He took his M.B., B.S. at Hong Kong University in 1928, and returned to Malaya to practise. He had always taken an active part in the public life of the settlement, where he served as municipal commissioner. He was nominated to the Advisory Council of the Malayan Union in April, 1946, and continued as a member of the Federal Legislative Council after its formation. He was also a member of the Federal Executive Council. He had been President of the Penang Rotary Club, and served as an officer of the Chinese Company of the Penang and Province Wellesley Volunteer Corps. Last year Dr. Ong attended the United Nations Organization Educational Conference in Nanking as a delegate from Malaya. Dr. Ong had been a member of the British Medical Association for many years.

Dr. BERNARD RAYNE PARMITER died in Wimborne Cottage Hospital, of which he was a medical officer, after a short recurrence of a previous illness on Aug. 19, at the age of 62. Educated at Dover College and Guy's Hospital, he qualified L.R.C.P., M.R.C.S. in 1911 and graduated M.B., B.S. in the following year. He held house appointments at Guy's Hospital, the Evelina Hospital for Sick Children, and at the Brompton and Lewisham Hospitals. During the 1914–18 war he served as a captain in the R.A.M.C. for four and a half years in Egypt, Gallipoli, Macedonia, Palestine, and after the armistice in Constantinople and Asia Minor. Coming to Wimborne as a partner in general practice in 1920, he took a keen interest in many aspects of the life of the community, and became greatly loved by the people around for his personal qualities as well as for his professional skill. He was public vaccinator for the Wimborne Rural Area, medical officer to the Wimborne Infirmary, and medical officer to St. Christopher's Children's Home. There the children watched eagerly every Tuesday afternoon for Dr. Parmiter's car. The shyest of them would be put at ease, and laughing and talking to him in a very few minutes. He entered into all their fun and will be sorely missed. The older children will always carry with them memories of his unfailing kindness. Outside his purely professional work he found time to be a member of the town council and its chairman in 1928–9, a churchwarden of Wimborne Minster, and president of the local branch of Toc H. His happiest recreation and interest was perhaps the Boy Scouts, of which he was the district president. For many years he spent part of his holiday in camp with them, and had always been closely associated with the movement. Last April he was invested on behalf of the Chief Scout with the gold medal of merit for forty years' outstanding service. He served on the Dorset Panel Committee and Dorset Medical Service Committee for many years until stricken in 1945 with the malady which was later to cause his death.

Medico-Legal

DAMAGES AGAINST AN ORTHOPAEDIC SURGEON

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

A mishap with plaster-of-Paris resulted in an action in the Manchester Assize Court being settled for £7,000 damages against Mr. Ian Douglas Kitchin, a surgeon of the Lancaster Royal Infirmary. Dr. Cecil Gould, a general practitioner, was also sued but exonerated.[1] The evidence showed that the father of a boy of five consulted Dr. Gould about the child's knock-knees and was referred to Mr. Kitchin. The boy was admitted to the infirmary, and the father was assured that the operation would be a perfectly simple manipulation of the knees and an encasement in plaster. After a week the boy came home. He was obviously distressed and was awake during the night, constantly kicking out with his right leg. The father found the toes were white and the foot cold, and saw signs of gangrene. Dr. Gould examined the boy and said that he could not do anything about the leg; the plaster was tight but it was the surgeon's job; it would be all right and he would return in the morning. He paid another visit the next day and said the plaster seemed to be tight. When the father returned from work the boy was in agony, and he cut away part of the plaster to give him relief. Next day he took him back to hospital. Mr. Kitchin was very angry that the plaster had been touched and said that the child must come in again. Four days later the new plaster was covered with blood. For a month after discharge the child was taken regularly to the hospital as an out-patient, and about four new casts were put on the leg. The father by this time was in something like despair and asked that Professor McMurray be called in, but Mr. Kitchin would not agree, saying, "You need not worry; when I have made a mistake I will let you know." In the result the boy's foot was paralysed and the calf muscle practically wasted away.

Mr. Henry Poston, a Manchester surgeon, said that the cause of the boy's condition was the tight fitting of the plaster. If the plaster had been removed on the day after the boy first returned from the hospital there would have been no disability, but if it had been left until the next day a pressure ulcer would have formed. Mr. D. L. Griffiths, an orthopaedic surgeon, said that there was a strong chance that the right leg would have to be amputated.

Mr. Kitchin, giving evidence, said that when the boy was first discharged there was a chance for his recovery. After seeing the leg later he realized that some damage had been done but thought that a good useful leg could still be obtained. He agreed with the judge's suggestion that the seed that had brought about the present condition of the boy had existed on his return to the hospital three days after his first discharge. The treatment when the boy was in hospital for the second time was to allow the abscess to drain and continue if the drainage was clear. Asked whether it would not have been a good idea to try penicillin earlier, he replied that at that time he would not

[1] *Lancaster Guardian*, May 14.

use it until he could locate the abscess, but now it was used blind. When the boy was brought back with the plaster cut there was no sign of an abscess, though he thought one was present. Later it presented on the lateral side of the calf. When he first saw the boy he thought an osteotomy for knock-knee would be necessary, but after some months there was an improvement and only manipulation was required. When the boy was discharged for the first time he was perfectly well and did not complain of pain. Some restlessness during the night was caused by the rubbing of the plaster at the top of the leg. The circulation was good and the plaster not tight. When his father brought him back he was obviously ill: he was flushed and had a well-marked bronchitis. The toes of the right leg were slightly swollen and faintly bluish. The leg which was swollen had been under tension, but Mr. Kitchin could not find a cause for the pressure. Some damage had been done at that time, and he decided to watch the leg. There was some blistering of the leg after removal of the plaster, a not uncommon happening. He could not recall the father pressing for a second opinion. When the child was brought back as an in-patient for the third time the foot was reinfected.

On entering judgment for the amount agreed, the judge remarked that it was always an extremely painful matter to try a case against a professional man. Everyone, with the best will in the world, made mistakes. There had been no complaint here of lack of professional zeal. Mr. Kitchin might have formed an erroneous conclusion, but there was no scintilla of suggestion of any sort of unethical conduct from start to finish. Obviously Dr. Gould, against whom the case had been withdrawn, was not in any way responsible. He had nothing to do with the operation, the plaster, or the treatment. The boy had come out of a first-class hospital with the highest specialist treatment and technical skill, and he would have been taking a very grave risk if he had taken the law into his own hands and done anything with the plaster.

Universities and Colleges

UNIVERSITY OF CAMBRIDGE

George Fulton Roberts, M.B., B.Chir., and Norman Boyne Finter, M.B., B.Chir., have been appointed University Demonstrators in Pathology for three years from Oct. 1.

Raymond Seidelin, B.M., B.Ch., has been elected to an Elmore Medical Research Studentship from Sept. 1.

UNIVERSITY OF GLASGOW

George Lightbody Montgomery, T.D., M.D., Ph.D., F.R.F.P.S., has been appointed to the St. Mungo-Notman chair of pathology, associated with the Royal Infirmary, Glasgow, in succession to Professor John William Stewart Blacklock, M.D., F.R.F.P.S.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW

At a meeting of the Royal Faculty of Physicians and Surgeons of Glasgow held on Sept. 6, with Professor Geoffrey B. Fleming, president, in the chair, the following were admitted Fellows of Faculty *qua* Physician: J. B. Cochran, J. E. A. David, M. M. Desai, T. Jack, P. MacArthur, R. C. MacGillivray, W. G. Manderson, R. A. Peebles-Brown, N. Sher. The following were admitted Fellows of Faculty *qua* Surgeon: J. T. S. Buchan, R. W. Busschau, T. L. Chapman, G. L. Clark, J. R. Hutchinson, J. D. Joubert, A. B. Kothari, W. S. Mack, Pearl A. I. MacLeod, A. M. Porter, W. Rankin, C. J. Slight, W. B. Stirling, A. E. Wilkinson, R. B. Wright.

The Nurseries and Child Minders Regulation Act recently received the Royal Assent, and in Circular 143/48 the Ministry of Health draws the attention of local health authorities to their duties under the Act. From now on all premises used as day nurseries must be registered, and persons who take children under 5 into their own homes for the day and receive payment for this must also be registered. Local health authorities may lay down conditions about the administration of day nurseries, and about the number of children who may be received in a daily minder's home. Similarly requirements about medical supervision of the children and the taking of precautions against infectious disease may be imposed. This new duty of local health authorities will stand referred to the health committees recently set up under the National Health Service Act.

Medical News

World Medical Association

At the meeting of the General Assembly of the World Medical Association in Geneva last week Dr. Charles Hill, Secretary of the British Medical Association, was made President-Elect for the year 1949–50. The General Assembly will meet again in London in the autumn of 1949.

W.M.A. Bulletin

Dr. Morris Fishbein, Editor of the *Journal of the American Medical Association*, has agreed to serve as Editor of the *W.M.A. Bulletin*, which will be published in the U.S.A.

Higher Pay for Student Nurses

The Nurses and Midwives Whitley Council has agreed that student nurses, pupil assistant nurses, and pupil midwives employed in the National Health Service shall receive increased allowances from Sept. 1. A first-year student in general training receives £200 a year plus dependants' allowances and meals on duty. The cash allowance is £100 (an increase of £30), and the emoluments are valued for superannuation at £100. Dependants' allowances are 10s. a week for an adult and 5s. for the first child. Payment in the second year of training is £210 plus £5 on passing the preliminary examination. In the third year it is £225. The first-year rate for pupil or probationer assistant nurses is £200 plus dependants' allowances, and for the pupil midwife who is a State-registered nurse £230 (not State-registered, £205). The provisional rate for the post-registration student nurse with three years' training is £230 in the first year. Students living out are allowed free meals on duty, uniform, and laundry in addition to their allowances. A special committee is considering the remuneration of student mental nurses and student nursery nurses.

Rockefeller Travelling Fellowships in Medicine

The Medical Research Council announces that Rockefeller Travelling Fellowships in Medicine for the academic year 1948–9 have been awarded as follows: Dr. K. W. Donald, Medical Professorial Unit, St. Bartholomew's Hospital, London; Dr. L. P. R. Fourman, Nuffield Department of Clinical Medicine, University of Oxford; Dr. R. H. Girdwood, Department of Medicine, University of Edinburgh; Dr. A. Isaacs, Department of Medicine, University of Sheffield; Mr. A. I. S. Macpherson, Department of Surgery, University of Edinburgh; Dr. H. B. Stoner, Department of Pathology, University of Sheffield; Mr. S. F. Taylor, Department of Surgery, Postgraduate Medical School of London.

Study of Tumours

The Committee on Pathology of the American National Research Council has appointed a subcommittee on oncology with the following members: Dr. Shields Warren (chairman), Dr. Balduin Lucke, Dr. Fred Stewart, Dr. Harold Stewart, Dr. Arthur P. Stout, Dr. Milton C. Winternitz, Dr. Howard T. Karsner (chairman of Committee on Pathology, *ex-officio*). Brig.-Gen. Raymond C. Dart, Director of the Army Institute of Pathology, is co-operating with the committee and making the institute's facilities and resources available and is providing office space for the permanent secretary. The aims of the subcommittee are: (1) improvement in the teaching of oncology; (2) dissemination of information on oncology to clinical pathologists, students, and teachers of oncology; (3) the establishment of criteria for diagnosis of tumours; (4) the simplification of terminology by recommending a single term for each tumour and listing separately the appropriate synonyms.

Oculist to the Princess Royal

Mr. B. W. Rycroft has been appointed oculist to H.R.H. the Princess Royal.

Mental Health of Children

To help the development of an international organization for the mental health of children an office has been opened at 30, West 58th Street, New York City, to which inquiries should be addressed. The following officers of the council have been elected: Dr. Leo Kanner, Johns Hopkins University School of Medicine (president); Dr. M. Tramer, editor of the *Internationale Zeitschrift für Kinderpsychiatrie* (vice-president); Dr. Ernest Harms, editor of the *Nervous Child* (acting secretary).

Wills

Sir George Francis Blacker, of Frensham, Surrey, late of University College Hospital, left £44,424. Dr. John McMyn, of Kirkcudbright, left £3,852. Dr. John Gutch, of North Walsham, Norfolk, left £53,474.

COMING EVENTS

Conference on Dust in Industry

The Society of Chemical Industry has organized a conference on Dust in Industry to be held at the University of Leeds from Sept. 28 to 30. On Thursday, Sept. 30, commencing at 9.30 a.m., the following papers relating to medical subjects will be delivered: "Tetryl Dermatitis and Its Prevention," by Professor W. M. Cumming and I. A. Brownlie; "Recent Advances in the Study and Treatment of Silicosis," by Professor E. J. King, M.A., D.Sc.; "Manganese Pneumonitis," by Dr. T. A. Lloyd Davies; "Arsenical Dust in Industry," by Dr. A. M. Currie, M.A.; "A Positive Method for the Determination of Free Silica in Dusts," by Professor A. L. Roberts, Ph.D.; "La Pénetration Pulmonaire des Toxiques Industriels: Exemple du Bioxyde de Manganese," by Le Doyen Professor R. Fabre; "Cancer of the Lung and Cancer of the Nose," by Dr. A. J. Amor; "Idle Thoughts on the Pneumoconioses," by Dr. E. R. A. Merewether, C.B.E., M.D., F.R.C.P., F.R.S.Ed. Attendance at the conference is free to members of the Society, who may obtain a set of preprints of the papers for 10s. 6d.; others will be admitted on payment of £2 2s. for a set of preprints. Those wishing to attend are asked to advise the general secretary of the Society at 56, Victoria Street, London, S.W.1, as soon as possible, and also to state whether accommodation will be required. A special dinner will be held at the Queen's Hotel, Leeds, on Tuesday, Sept. 28, for those attending the conference. Tickets (price 21s. including wines) are available from Dr. J. E. Garside, at Leeds University, and early application is desirable.

Smoke Abatement

The annual conference of the National Smoke Abatement Society will be held at Cheltenham from Sept. 30 to Oct. 1. The Minister of Fuel and Power, Mr. Hugh Gaitskell, will address it. The Society will present a preliminary report on the survey of the sources and incidence of atmospheric pollution. Particulars may be obtained from the Society, Chandos House, Buckingham Gate, London, S.W.1.

Royal College of Obstetricians and Gynaecologists

Dr. Emil Novak, Associate in Gynaecology, The Johns Hopkins Medical School, Baltimore, U.S.A., will deliver a lecture "On Certain Functioning Tumours of the Ovary" at the College (58, Queen Anne Street, London, W.), on Friday, Oct. 1, at 2.15 p.m. The lecture is awarded under an endowment by a Fellow of the College for "a lecture to be given every fourth year by an American gynaecologist of merit to cement more closely the bonds of friendship between the British Empire and the U.S.A., and as a token of gratitude for their help in the darkest hours of the World War." Admission is by ticket only, obtainable from the secretary of the College.

William Blair Bell Memorial Lecture

A William Blair Bell Memorial Lecture will be delivered by Newell Willard Philpott, M.D., C.M., F.A.C.A., F.R.C.S.(Can.), F.R.C.O.G., Professor of Obstetrics and Gynaecology, McGill University, Montreal, Canada, at the Royal College of Obstetricians and Gynaecologists (58, Queen Anne Street, London, W.) on Saturday, Oct. 2, at 10 a.m. His subject is "Rhesus Factor Iso-immunization and Haemolytic Disease of the Newborn." Admission is by ticket only, obtainable from the secretary of the College.

Hunterian Society

The annual party of the Hunterian Society will be held at Gunters' Restaurant, 6, Stanhope Street, Park Lane, London, W., on Monday, Oct. 4, from 6 to 8 p.m. Fellows are asked to apply as soon as possible for invitation cards, price 15s. each, for themselves and their guests, to Dr. Kenneth McFadyean, 74, Herne Hill, London, S.E.24.

Postgraduate Lectures on Modern Therapeutics

A course of ten postgraduate subscription lectures on modern therapeutics will be delivered at the Society of Apothecaries of London (Black Friars Lane, Queen Victoria Street, E.C.) at 5 p.m. beginning on Oct. 18 and ending on Nov. 5. The fee for the whole course is £3 3s., single lectures 7s. 6d. Details will be published in the diary column of the *Journal* week by week.

Annual Harveian Commemoration

The Royal College of Physicians of London will hold a dinner at the College, Pall Mall East, S.W., on St. Luke's Day, Monday, Oct. 18, at 7.30 for 8 p.m. The contribution payable by each Fellow is 10s. and those wishing to attend should notify the Registrar not later than first post on Oct. 1. The dinner is confined to Fellows and there will be no guests.

SOCIETIES AND LECTURES

Wednesday

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—At 28, Portland Place, London, W., Sept. 22, 3 p.m. "*The Surgical Treatment of Gastric Ulcers.*" The Bengué Memorial Award Lecture for 1948, by Dr. Paul Banzet.

Friday

BIOCHEMICAL SOCIETY.—At Department of Biochemistry, The University, Sheffield, Sept. 24, 11.30 a.m., 269th meeting. Papers will be read.

SURREY COUNTY MEDICAL SOCIETY.—At Farnham County Hospital, Sept. 24, 7 p.m. Clinical meeting.

APPOINTMENTS

Drs. E. Y. Laurent, C.M.G., A. E. De Chazal, O.B.E., and J. M. Curé have been appointed Members of the Legislative Council of the Colony of Mauritius.

Alexander James Smith McFadzean, M.B., Ch.B., M.R.C.P., has been appointed Professor of Medicine in the University of Hong Kong.

Dr. McFadzean, who is 34, qualified in 1936 at Glasgow University and took the M.R.C.P.Lond. in 1946. He is at present lecturer in medicine at Glasgow University.

Brian Brendan Hickey, M.A., B.M., M.Ch., F.R.C.S., has been appointed Director of Surgery to the Morriston Emergency Hospital, Swansea.

Mr. Hickey graduated in 1935 after training at Oxford University and the London Hospital. For the last two years he has been Surgeon to the Iraq Government. He recorded a case of blast injury in this *Journal* in 1945, **2**, 218.

BENTHAM, F., M.B., B.S., D.P.H., R.C.P.S., Medical Officer of Health for Kettering.

EASTWOOD, C. G., B.Sc., M.R.C.S., L.R.C.P., D.P.H., Medical Officer of Health for Cambridge.

JONES, D. J., B.Sc., M.B., B.Ch., D.P.H., Medical Officer of Health for Rugby and medical officer and divisional school medical officer.

PATERSON, M. B., M.B., Ch.B., Temporary Assistant Medical Officer of Health for Lanarkshire.

WALES, W. T. H., M.R.C.S., L.R.C.P., D.P.M., Deputy Medical Superintendent of Monmouthshire Mental Hospital.

WILDMAN, J. H., M.R.C.S., L.R.C.P., D.P.H., Medical Officer of Health, East Herts Combined Sanitary District.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Brownridge.—On Aug. 23, 1948, to Phyllis, wife of Dr. C. E. Brownridge, of Farndale, Almondsbury, near Bristol, a son.

Burgess.—On Sept. 11, 1948, at Ballard Lodge, Alverstoke, Hants, to Phyl (née Hewitt), wife of Surgeon Commander P. G. Burgess, R.N., a son.

Cutts.—On Sept. 1, 1948, in London, to Ailsa, wife of Dr. J. G. Cutts, a daughter.

Davis.—On Sept. 11, 1948, at St. Helier Hospital, Carshalton, to Marjorie, wife of Dr. H. Davis, a daughter—Rosalyn Celia.

Deacon.—On Sept. 2, 1948, at the Birmingham Maternity Hospital, to Sybil, wife of Mr. A. L. Deacon, F.R.C.S.Ed., M.R.C.O.G., a second son—Andrew Robert.

Middlemiss.—On Sept. 5, 1948, at Charing Cross Hospital, to Maria (née van Sasse van Ysselt), wife of Capt. J. L. Middlemiss, R.A.M.C., a daughter.

Rutter.—On Sept. 2, 1948, to Anne, wife of Dr. W. Rutter, of Netherfield House, Seghill, Northumberland, a son

MARRIAGES

Brown—Hardy.—On Aug. 27, 1948, at Great Sampford, Saffron Walden, Essex, Wilfred Stuart Brown, M.R.C.S., of Shrodells Hospital, Watford, to Betty Stella Hardy, of Great Sampford.

Sears—Conn.—On Sept. 4, 1948, at University Chapel, St. Andrews, Dr. Harold Trevor Newton Sears, M.B., M.R.C.P.Lond., of Tresidder, Mullion, Cornwall, to Dr. Janet Sorley Conn, M.B., Ch.B. (St. Andrews), of Kilnburn House, East Newport, Fife.

DEATHS

Banks.—On Sept. 9, 1948, at Hadlow Down, Sussex, Alfred Banks, F.R.C.S., aged 86.

Brooks.—On Sept. 9, 1948, at Manchester Royal Infirmary, Peter Brooks, M.B., Ch.B. aged 25.

Elder.—On Sept. 7, 1948, at 60, Rawlinson Road, Southport, George Tatham Davison Elder, M.R.C.S., L.R.C.P., aged 73.

Kempster.—On Sept. 7, 1948, at 46, Portland Court, Great Portland Street, London, W., Christopher Richard Kempster, M.R.C.S., L.R.C.P.

M'Vean.—On Aug. 31, 1948, as the result of a railway accident near Arbroath, Ronald Henderson M'Vean, M.B., Ch.B., Captain R.A.M.C.

Pulling.—On Sept. 9, 1948, at 11, Old Steine, Brighton, Herbert John Pulling, M.R.C.S., L.R.C.P., aged 88.

Soni.—On Sept. 7, 1948, suddenly, at his residence, 30, Wilmslow Road, Withington, Manchester, Mul Raj Soni, B.A., M.B., Ch.B., D.P.H., beloved husband of Edith Constance Soni.

Tuxford.—Recently, at Mayday Hospital, Reginald Tuxford, of Lower Addiscombe Road, Croydon, Surrey, aged 75.

Wheaton.—On Sept. 5, 1948, Samuel Walton Wheaton, M.D., F.R.C.P., of 16, Palace Road, Streatham Hill, London, S.W., aged 86.

Willis.—On Sept. 12, 1948, at Barnes Convalescent Hospital, Cheadle, Cheshire, Eugenie Leeson Willis, F.R.C.S., of 31, Wilmslow Road, Withington, Manchester, second daughter of Captain F. R. Willis, R.N. (Ret.), and Mrs. Willis, of the Knapp, Portesham, Dorset, aged 38.

No. 35

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended Aug. 28.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1948					1947 (Corresponding Week)				
	(a)	(b)	(c)	(d)	(e)	(a)	(b)	(c)	(d)	(e)
Cerebrospinal fever	29	4	14	1	—	32	4	32	2	2
Deaths		1	—				1	1		
Diphtheria	123	11	34	10	5	164	15	37	10	3
Deaths	1	1	1	—	—	—	—	—	1	—
Dysentery	70	9	55	5	—	85	8	12	—	—
Deaths				—	—				—	—
Encephalitis lethargica, acute	2	1	1	—	—	2	—	—	—	—
Deaths		—					—			
Erysipelas			28	15	1			35	5	2
Deaths		—					—			
Infective enteritis or diarrhoea under 2 years				40					107	
Deaths	24	—	10	1	2	69	7	20	6	2
Measles*	3,774	149	25	11	15	2,114	110	49	155	3
Deaths†			—	1	—	—	—	—	1	—
Ophthalmia neonatorum	55	6	10	—	—	51	5	21	—	—
Deaths										
Paratyphoid fever	17	3	1 (B)	—	—	33	4	4 (B)	—	2 (B)
Deaths	3	2	—	—	—	—	—	—	—	—
Pneumonia, influenzal	240	16	—	2	3	229	10	3	1	1
Deaths (from influenza)‡	4	1	—	—	—	4	—	—	—	—
Pneumonia, primary			95	16				112	14	
Deaths	99	9		1	3		19		6	7
Polio-encephalitis, acute	7	—				45	3			
Deaths							1			
Poliomyelitis, acute	70	6	3	2	—	612	77	172	10	15
Deaths§	3	—					—			
Puerperal fever		2	5		—		3	16		—
Deaths										
Puerperal pyrexia‖	100	8	10	—	—	122	11	12	—	—
Deaths		—					—			
Relapsing fever	—	—			—	—	—			—
Deaths										
Scarlet fever	812	42	191	52	17	436	34	83	18	18
Deaths†			—	—	—	—	—	—	—	—
Smallpox	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Typhoid fever	12	1	3	—	—	11	3	3	2	1
Deaths	—	—	—	—	—	—	—	1	1	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Whooping-cough*	3,162	248	60	48	8	1,618	193	75	59	6
Deaths	7	2	—	—	—	9	1	3	—	—
Deaths (0–1 year)	247	32	37	10	7	330	44	70	24	16
Infant mortality rate (per 1,000 live births)										
Deaths (excluding still-births)	3,955	619	533	134	91	3,678	578	561	159	106
Annual death rate (per 1,000 persons living)			10·8	8·4				11·7	10·0	
Live births	7,298	1234	903	398	236	8,377	1331	1001	392	259
Annual rate per 1,000 persons living			18·2	24·9				20·2	24·7	
Stillbirths	222	18	30			227	25	37		
Rate per 1,000 total births (including stillborn)			32					36		

* Measles and whooping-cough are not notifiable in Scotland, and the returns are therefore an approximation only.

† Deaths from measles and scarlet fever for England and Wales, London (administrative county), will no longer be published.

‡ Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

§ The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, London (administrative county), are combined.

‖ Includes puerperal fever for England and Wales and Eire.

EPIDEMIOLOGICAL NOTES

Typhoid at Oswestry

The cause of the outbreak of typhoid fever at the Shropshire Orthopaedic Hospital at Oswestry has not yet been established. The investigators have been handicapped by the fact that so far it has not proved possible to type the infecting organism. One nurse who has had no symptoms has been shown to be excreting typhoid bacilli, but at the moment it does not seem likely that this was the original source of infection. There have been no cases in the nearby town or in the area surrounding the hospital. Up to Sept. 13 there had been 33 cases isolated: 25 of these patients are members of the resident staff—the majority of them nurses or ward-maids; 5 are bed patients; and 3 are members of the non-resident staff of the hospital.

Discussion of Table

In *England and Wales* there was a fall in the number of notifications of measles 837, whooping-cough 98, and dysentery 41, and the only rise of any size was 76 for scarlet fever.

Variations in the local trends of scarlet fever were quite small and the increase in incidence was mainly in the northern section of the country. The largest decreases in the returns for measles were Yorkshire West Riding 133, Gloucestershire 95, Northumberland 92, Bedfordshire 79, and Essex 64. The notifications of whooping-cough in London were 67 fewer than in the preceding week, but in all other areas little change was reported. The returns of diphtheria showed no variation of any size from the preceding week.

The decrease in the incidence of dysentery was mainly contributed by Lancashire, where the notifications declined from 40 to 9. The largest returns of dysentery during the week were Yorkshire West Riding 15 (Sheffield C.B. 12), and Surrey 10 (Coulsdon and Purley U.D. 8). The increase in the notifications of acute poliomyelitis recorded last week was maintained; the largest centres of infection were Lancashire 7, London 6, Essex 6, Surrey 4, and Middlesex 4.

In *Scotland* increases were reported in the notifications of scarlet fever 57, whooping-cough 36, and diphtheria 11. Most of the increased incidence of diphtheria was contributed by Glasgow, where over one-third of the total cases were notified. A rise in the incidence of scarlet fever was reported from most areas of the country.

In *Eire* infectious diseases were less prevalent during the week, and the falls included whooping-cough 66, measles 28, and scarlet fever 22. The notifications of diarrhoea and enteritis were 5 fewer for the whole country, but an increase of 5 was reported in Dublin C.B.

In *Northern Ireland* falls were recorded in the notifications of measles 10, whooping-cough 9, and scarlet fever 5. The first two diseases reflect the trend in Belfast C.B., but the incidence of scarlet fever increased by 5 in this city during the week.

Quarterly Return for Scotland

The birth rate during the second quarter was 20.7, which was 0.5 above the average of the five preceding June quarters. The infant mortality was 43 per 1,000 registered live births and was 11 below the five years' average. Maternal mortality was 2.6 per 1,000 live births, being 0.1 above the rate for the June quarter of 1947 but 0.9 below the five years' average. The general death rate was 11.4 per 1,000 and was 0.8 below the rate for the second quarter of 1947 and 0.6 below the average of the five preceding June quarters. Deaths from the principal epidemic diseases included: 25 from measles, 19 from influenza, 14 from whooping-cough, and 10 from cerebrospinal fever. The death rate for all forms of tuberculosis was 84 per 100,000, and for respiratory tuberculosis 71. The former rate is 2 below that for the second quarter of 1947, but the latter is 3 above.

Week Ending September 4

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 734, whooping-cough 2,996, diphtheria 105, measles 2,962, acute pneumonia 246, cerebrospinal fever 29, acute poliomyelitis 70, dysentery 64, paratyphoid 11, and typhoid 9.

The annual report for 1947 of the Medical Research Council of Ireland gives some account of the work of a number of special committees, notably those concerned with chemotherapy, goitre, and B.C.G. The Council's grant for general research has been increased from £5,000 to £10,000 a year, and there is also a special grant of £6,000 for investigation into the chemotherapy of tuberculosis. It is expected that the scheme for B.C.G. vaccination recommended to the Minister for Health will be put into operation this year.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Infestation by "Harvesters"

Q.—*Is there any effective protection against infestation by "harvesters," which makes life in the country in the late summer quite miserable for many people? The insects, which I presume are in the larval stage, seem to be harboured by rough grasses; they burrow under the skin, particularly in the axillae, upper arms, and other parts where the skin is soft, and set up intense irritation. The very fine thread-like larva can be removed with a needle. All the usual insect repellents have been tried, but none of them seems to be effective.*

A.—Attacks of harvest mites (*Trombicula autumnalis*) certainly cause great discomfort to sensitive people, who probably constitute the great majority. The larvae of these mites are parasitic on wild rodents and birds and sometimes attack other animals or man. They crawl up the limbs and usually halt where a tight constriction of the clothing obstructs their further progress; here they embed their mouthparts and feed. After a few days they drop off the host to the soil and pass the remainder of their lives in a harmless free-living state. The repellent dimethyl phthalate should be effective against this pest. An ointment containing about 40% of dimethyl phthalate should be rubbed over exposed limbs; this should prevent attacks for several hours or perhaps a day. Alternatively, undiluted dimethyl phthalate can be smeared over the socks or stockings, and perhaps also the cuffs, collars, and other openings of the clothing. The liquid should not be applied to artificial silk.

Delivery after Operation for Prolapse

Q.—*A woman now in the sixth month of her third pregnancy had an operation for prolapsus uteri and lacerated cervix one year after the birth of her second child four years ago. The cervix is normal in size and position, but there is a fibrosed scar along the anterior surface. Should she be delivered in her own home?*

A.—Several considerations are involved here, and much depends on what operation was performed on the cervix. If it was amputated, and particularly if the amputation was high, premature labour is likely to occur. Difficulty in dilatation of the cervix is a rare but nevertheless real possibility, irrespective of the height of the amputation. Other operations on the cervix are less likely to interfere with uterine function, although any scar which extends deeply may cause premature labour. Another important aspect of this case is the need to take all possible steps to minimize the chances of a recurrence of prolapse. These include a liberal episiotomy (even though it appears unnecessary) followed by its accurate repair and the avoidance of delay in the second stage of labour. Difficulties to be anticipated are the care of a premature baby (possible), cervical dystocia (rare), and repair of an extensive episiotomy incision (inevitable). The disposal of the patient depends on where these difficulties can be most efficiently overcome, and this in turn depends on the conditions of the patient's home, the availability of assistance, and the standard of the hospital facilities in the neighbourhood. Assuming the latter are good, then as a general rule it would not be in the best interests of the mother or child for the confinement to take place at home.

Undulant Fever

Q.—*What is the latest treatment for undulant fever contracted in England? The patient is an elderly doctor who periodically suffers great discomfort and pain with the raised temperature.*

A.—No really long and well-controlled series of cases of brucellosis has been investigated. The following drugs have been known to bring about the termination of symptoms. (1) Neoarsphenamine: two or three injections intravenously at weekly intervals. (2) Sulphonamides, especially sulphadiazine: 6 g. a day for three weeks occasionally brings about cure. (3) Sulphadiazine and streptomycin combined: streptomycin, 2 to 4 g. daily for 7 to 25 days; sulphadiazine, 4 g. initially followed by 1 g. four-hourly for three weeks (Spink, Hall, Shafer, and Brande, *J. Amer. med. Ass.*, 1948, **136**, 382). (4) "Antrypol" (suramin): 1 g. intravenously once a week (contraindicated if the kidneys are not healthy).

Prevention of Ringworm of the Scalp

Q.—*A number of cases of ringworm of the scalp are occurring in the district and, as M.O.H., I wish to circularize the local barbers and advise them what to do should they accidentally clip a sufferer's head. Is there any reliable information on percentage strengths of, and minimum immersion periods in, commonly available disinfectants which will effectively destroy the ringworm fungus on barbers' instruments?*

A.—In an article by Schwartz and others (*J. Amer. med. Ass.*, 1946, **132**, 58) it is suggested that clippers could be sterilized without damage by working them for 10 seconds while immersed in petroleum oil (boiling-point 150 to 200° C.) at 100° C.; by boiling them for three minutes in a 2% saponated solution of cresol; or by immersing them in a 10% solution of this in the cold for 15 minutes. These methods of control led to a drop in incidence of ringworm of the scalp.

Difficult Delivery

Q.—*What is the obstetric condition in which the baby is presenting by the vertex, occipito-anterior, and there is no evident disproportion but the mother fails to deliver herself? On application of the forceps with more force than is conducive to one's peace of mind the baby emerges with the marks of the blades under the angle of the jaw on one side and over the parietal bone on the other, suggesting that the baby's head is inclined over towards one of its own shoulders rather than presenting squarely. I have delivered dozens in this condition and would rather deal with a straightforward occipito-posterior position, which, if diagnosed before the head becomes moulded to the wrong shape, is manually rotated and delivered with comparative ease. I have asked several eminent obstetricians about this condition, which I cannot find mentioned in any textbook, and they talk learnedly but vaguely about the head not being "properly flexed," but they make no suggestions about causation or what should be done.*

A.—The suggestion that in these cases the foetal head is laterally flexed on the trunk, with the occiput fully rotated anteriorly, is difficult to accept. This state of affairs is not likely to occur except when the foetal neck is deformed, and experiments carried out on a doll and pelvis indicate that if it were as described merely locking the forceps would suffice to correct it. The probable explanation of the observations recorded is the pelvic application of forceps when the foetal head is incompletely rotated—i.e., when it is still lying with the sagittal suture in one or other oblique diameter. This is a common experience and results in forceps marks on the foetal head roughly in the sites described in the question. The treatment of this condition depends on accurate diagnosis of the position of the foetal head followed by a cephalic rather than a pelvic application of forceps, with or without preliminary manual rotation of the occiput to the front.

Pteroyldiglutamic Acid in Malignant Disease

Q.—*Are pteroyldiglutamic acid and pteroyltriglutamic acid of value in malignant disease? Has any work similar to that of Leuchtenberger and Farber been done in the United Kingdom, and is any hospital now working along these lines?*

A.—While earlier reports conveyed some indication of ameliorative effects from the treatment of malignant disease with pteroyldiglutamic acid and pteroyltriglutamic acid, such effects do not seem to have been confirmed in later clinical work whether in this country or in the United States. Demonstrable even if slight activity of this kind would still be of interest for the problem of tumour chemotherapy from the experimental aspect, but it seems clear that any such activity which these compounds possess is far short of rendering them of value in clinical practice.

Venereal Disease

Q.—*What has been the peak rate of syphilis and gonorrhoea in the B.A.O.R. since the end of the war? Is the increase in the incidence in venereal disease shown in the Ministry of Health Report for the year 1946 likely to be a peak figure, or has there been a further rise in 1947? Can any explanation be offered for the fact that this expected post-war rise in venereal disease is delayed as compared with the corresponding rise after the 1914–18 war? Is it true that the spirochaete can be transmitted in the seminal fluid for three to five years after a supposed "cure"? How long after the cure of syphilis is marriage permissible?*

A.—Figures for syphilis and gonorrhoea rates in the B.A.O.R. up to date are not available, but probably the highest were reached in 1946, when for one quarter they were in the neighbourhood of an equivalent annual ratio of 80 to 90 per 1,000. The civilian rates in this country for fresh infections with syphilis and gonorrhoea during 1947 fell well below those for 1946. If it is admitted that the expected post-war rise in V.D. was delayed longer after the 1939–45 war than after the 1914–18 war, and it is not so clear that it was, there are many possible explanations, none of which is very convincing. Spirochaetes have been demonstrated in the seminal fluid of latent syphilitics some years after the date of infection; such persons would presumably be able to transmit their infection. It is usually considered safe to allow a syphilitic person to marry when five years have elapsed from the time of infection, but in the case of a syphilitic woman it is wise to recommend antisyphilitic treatment during any pregnancy in order to ensure the birth of a non-syphilitic child.

Treatment of Diverticulitis

Q.—*How should one treat loss of weight and increasing constipation in a case of diverticulitis of the lower colon? A man aged 57 had been diagnosed by a competent radiologist as suffering from diverticulitis. He still plays golf and tennis. Most of his teeth have been extracted, and it is only within the last year that he has suffered from increasing constipation. He now complains of flatulence and abdominal discomfort after defaecation—his bowels never seem to be properly emptied. He has lost over 1 st. (6.35 kg.), and his weight is now 10 st. 5 lb. (65.77 kg.). Myalgia and weakness are present in both groups of extensor muscles of the thighs. He eats anything except food containing "roughage," and takes emuls. paraff. liq. c. phenolthal., two dessertspoonfuls every night. Is there any other treatment, and what is the prognosis?*

A.—The general symptoms of which this patient complains are severe for simple diverticulosis, even when accompanied by diverticulitis; obviously the possibility of carcinoma must be considered. The description suggests that the lesion would be within view of the sigmoidoscope. Provided malignant disease has been excluded, the indications are to maintain regular evacuations with liquid paraffin and a low residue diet. It sounds as though these measures were now losing their efficacy and that recurrent episodes of partial obstruction were taking place, hinting at a progressive stenosis of the bowel's lumen. If this is so, surgical treatment will become necessary, and it would be advisable to consult a surgeon before complete obstruction supervenes and the patient's health deteriorates further.

Dangers of Cinchophen

Q.—*I have been warned of the danger of using cinchophen for the removal of excess uric acid in the blood. Can you suggest any safer alternative? What are the principal dangers of cinchophen?*

A.—Cinchophen is the only efficient substance to increase the excretion of uric acid. Its principal danger is that it may cause hepatitis, and this has been known to go so far as to cause jaundice and death. This is, however, a very rare occurrence. In 1931 White estimated the annual consumption of cinchophen in the United States to be 90,000 lb. (40,823 kg.), so that the proportion of cases in which liver damage occurs must be very low. Cinchophen irritates the stomach, therefore while it is being used sodium bicarbonate should also be given (though not simultaneously); on the first day 15 g. (225 gr.) of sodium bicarbonate and 5–10 g. on the following days. This also keeps the urine alkaline. Plenty of fluid should be taken. Other points about the toxicity of cinchophen were discussed in a question and answer published on Aug. 28 (p. 450).

Hypoplastic Anaemia

Q.—*Are x-ray therapy, electrotherapy, sulphonamides, or residence or a visit to the Tropics contraindicated in cases of hypoplastic anaemia?*

A.—In cases of hypoplastic anaemia there is no contraindication to electrotherapy. Residence in the Tropics is contraindicated only in so far as it carries some additional risk of disease—e.g., amoebic dysentery—which a person with hypoplastic anaemia could less well support. *X*-ray therapy is contraindicated, although evidently there are circumstances in which it would be better to have *x* rays and risk the possible ill effects on the bone-marrow rather than go without them and suffer still worse effects. Much the same considerations apply to the use of sulphonamides; certainly one would not use them unless the patient had an infective condition which had failed to respond to penicillin and other measures.

NOTES AND COMMENTS

When was Hughlings Jackson Born?—Dr. E. H. DERRICK (The Queensland Institute of Medical Research, Brisbane) writes: Although authorities agree that Hughlings Jackson was born at Green Hammerton, in Yorkshire, they disagree as to whether this auspicious event occurred in 1834 or 1835. Supporters of 1834 are Power and Thompson's *Chronologia Medica*, Garrison's *History of Medicine*, and Dorland's and Gould's Medical Dictionaries. On the other hand the obituary in the *British Medical Journal* (1911, **2**, 950) and Bailey and Bishop's *Notable Names* give 1835. The Section of Neurology of the Royal Society of Medicine celebrated the centenary on April 4, 1935 (*Journal*, 1935, **1**, 769). This disagreement about such an illustrious figure is surprising. Can it be authoritatively settled?

Air Conditioning.—Lieutenant-Colonel H. G. G. ROBERTSON writes from Hamburg: In "Any Questions?" (Aug. 14, p. 363) a correspondent asks about air conditioning. Perhaps the following brief outline of the principles of air conditioning may be helpful. By means of a pump air is drawn from outside through a filter which rids it of gross particles. It is then passed through a screen of sprayed water at a temperature well below that which is finally required of the air. This washes it, cools it, and raises its humidity to saturation point. The air is then heated to the desired temperature, and, as hot air is capable of absorbing more water vapour than cold air and the actual amount of water remains the same, the relative humidity falls. By suitably adjusting the temperature of the cooling water it is possible to obtain almost any desired temperature and relative humidity in the air that enters the room. It is, of course, essential that doors and windows be kept closed to prevent the entry of the outside air.

Corrections

In amplification of its statement on the "Streptomycin Treatment of Tuberculosis" the Ministry of Health adds that streptomycin will nevertheless still be available for the treatment in any hospital of cases of acute miliary, meningeal, and ulcerative tracheo-bronchial and laryngeal tuberculosis, but in special instances applications for it should now be made to one of the Regional Distribution Centres instead of, as formerly, to the Ministry of Health.

Messrs. Henry Kimpton inform us that they are the English agents for *Clinical Laboratory Methods and Diagnosis*, by R. B. H. Gradwohl, noted in "Books Received" (Sept. 4, p. 478), and that the price is 10 guineas.

We regret that owing to a printing error the name of Mr. John Gilroy, who painted the presentation portrait of Sir John Herbert Parsons (Sept. 11, p. 529), was mis-spelt.

Dr. M. H. LOGG (Medical Superintendent, Grove Park Hospital, London, S.E.12) writes: Referring to the announcement regarding the distribution of streptomycin in your issue of Sept. 11 (p. 527) I would call your attention to the fact that the telephone number of Grove Park Hospital is Lee Green 1077—and not as printed, Lee Green 1547 (which happened to be the earlier telephone number until 1946).

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